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**UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA**

BIOSUCCESS BIOTECH, CO., LTD.,

Plaintiff,

v.

RICH PHARMACEUTICALS, INC., a
Nevada Corporation formerly known as
Nepia, Inc., IMAGIC, LLC, a California
LLC, RICHARD L. CHANG HOLDINGS
LLC, a New Jersey LLC, BEN CHANG,
an individual, and DOES 1 through 10,
inclusive,

Defendants.

Lead Case No. CV13-01340 JAK
(ANx)

[[Consolidated Case No. CV14-
00310 JAK (ANx)]]

**FIRST AMENDED COMPLAINT
FOR:**

- 1. PATENT INFRINGEMENT**
- 2. COPYRIGHT INFRINGEMENT**
- 3. MISAPPROPRIATION OF TRADE SECRETS**
- 4. BREACH OF FIDUCIARY DUTY**
- 5. STATUTORY UNFAIR COMPETITION**
- 6. COMMON LAW UNFAIR COMPETITION**
- 7. VIOLATION OF CAL. PENAL CODE SECTION 502**
- 8. TRESPASS TO CHATTELS**
- 9. INDUCING BREACH OF CONTRACT**
- 10. INDUCING BREACH OF FIDUCIARY DUTY**
- 11. CONVERSION**
- 12. CONSPIRACY**
- 13. AIDING AND ABETTING**

JURY TRIAL DEMANDED

1 Pursuant to Rule 15, Plaintiff Biosuccess Biotech Co. Ltd., (“Plaintiff” or
2 “Biosuccess”) submits its First Amended Complaint and alleges the following
3 against Defendants RICH PHARMACEUTICALS, INC., IMAGIC, LLC,
4 RICHARD L. CHANG HOLDINGS LLC, BEN CHANG, and DOES 1 through 10,
5 inclusive.

6 **PARTIES**

7 1. Plaintiff Biosuccess Biotech, Co., Ltd. (“Biosuccess”) is a corporation
8 organized under the laws of the Cayman Islands, with its principal place of business
9 in Taipei, Taiwan at Room 904, 9th Floor, No. 147, Sec. 2, Chien-Kuo North Road,
10 Taipei, Taiwan 10460, R.O.C.

11 2. On information and belief, Defendant Rich Pharmaceuticals, Inc.
12 (“Rich Pharmaceuticals”) is a corporation organized under the laws of the State of
13 Nevada, with its principal place of business at 9595 Wilshire Blvd., Suite 900,
14 Beverly Hills, California, 90212. Rich Pharmaceuticals was formerly known as
15 Nepia, Inc. (“Nepia”), a publicly traded corporation on NASDAQ, organized under
16 the laws of the State of Nevada as of August 9, 2010.

17 3. On information and belief, before July 2013, Nepia was engaged in
18 developing, manufacturing, and selling small boilers. On information and belief,
19 some time in 2012 or 2013, Rich Pharmaceuticals merged with Nepia. On or around
20 September 3, 2013, Nepia changed its name to Rich Pharmaceuticals, and now has
21 its principal place of business at 9595 Wilshire Blvd., Suite 900, Beverly Hills,
22 California, 90212.

23 4. On information and belief, Defendant Imagic, LLC (“Imagic”) is a
24 LLC registered in the State of California. Imagic’s agent for service of process is
25 Ben Chang, 9595 Wilshire Blvd., Suite 900, Beverly Hills, California, 90212.

26 5. On information and belief, Defendant Richard L. Chang Holdings LLC
27 (“RLC Holdings”) is a LLC registered in the State of New Jersey, with a place of
28 business at 107 Konner Avenue, Pine Brook, New Jersey 07058. On information

1 and belief, third party Richard L. Chang (“Richard Chang”) is an officer and
2 manager of RLC Holdings, and is a resident of Laguna Woods, California.

3 6. On information and belief, Defendant Ben Chang is an individual
4 residing at 312 North Mansfield Avenue, Los Angeles, California, 90036.

5 7. The true names or capacities of defendants named herein as DOES 1
6 through 10 are presently unknown to Biosuccess. Therefore, Biosuccess sues said
7 defendants by such fictitious names, and will amend this Complaint to show their
8 true names and capacities when the same has been ascertained. Biosuccess is
9 informed and believes, and based on such information and belief, alleges that
10 defendants sued as DOES 1 through 10, and each of them, are liable in whole or in
11 part for the wrongful acts alleged herein.

12 8. On information and belief, each Defendant, including DOES 1 through
13 10, inclusive, have willfully aided and abetted each of the other Defendants in the
14 wrongful concerted action described herein, or acted with or in furtherance of that
15 action, or assisted in carrying out its purpose alleged in this Complaint.

16 9. Defendants, and each of them, are individually sued as participants and
17 aiders and abettors in the wrongful conduct complained of herein, and the liability of
18 each arises from the fact that each has engaged in all or part of the improper acts,
19 plans, schemes, conspiracies, or transactions complained of herein.

20 **JURISDICTION AND VENUE**

21 10. This is a civil action for patent infringement arising under the laws of
22 the United States, 35 U.S.C. Section 1 *et seq.* This Court has subject matter
23 jurisdiction over such Federal Question claims pursuant to 28 U.S.C. Sections 1331
24 and 1338(a).

25 11. This Court also has Federal Question jurisdiction over the copyright
26 and unfair competition causes of action asserted in this Complaint pursuant to 28
27 U.S.C. Section 1338 and 17 U.S.C. Section 301(a).

28 12. Complete diversity exists between the parties, and the amount in

1 controversy exceeds \$75,000. Accordingly, subject matter jurisdiction is also
2 proper in this case under 28 U.S.C. Section 1332.

3 13. This Court has supplemental jurisdiction over any other claims asserted
4 in this Complaint pursuant to 28 U.S.C. Section 1367 and 1338(b).

5 14. Venue is proper in this Judicial District under 28 U.S.C. Sections 1391
6 and 1400(b).

7 15. This Court has personal jurisdiction over the Defendants because they
8 either residents of the State of California and/or have sufficient minimum contacts
9 such that the exercise of jurisdiction over each would not offend traditional notions
10 of fair play and substantial justice.

11 **FACTUAL BACKGROUND**

12 **A. Biosuccess is the Leader in TPA Research**

13 16. Founded in 2005, Biosuccess is a promising biomedical research and
14 development company dedicated to researching 12-O-tetradecanoylphorbol-13-
15 acetate, also known as “TPA,” for the treatment and applications of, *inter alia*, acute
16 myelogenous leukemia (“AML”), AIDS/HIV for patients who were refractory to
17 standard therapy, and stroke, among other applications. Biosuccess gave its TPA
18 production a unique designated name of “PD-616.” Biosuccess’s main goals are to
19 supply drugs to the global market and to obtain both domestic and foreign patent
20 protection.

21 17. Biosuccess has spent considerable time and effort, as well as millions
22 of dollars towards the research and development of PD-616 for the treatment of
23 AML and stroke, as well as numerous other treatment applications. Biosuccess has
24 developed and compiled valuable research and business data considered trade
25 secrets, as well as other confidential and proprietary information. Biosuccess’s
26 main research operations are based in China under the supervision of Dr. Zheng Tao
27 Han (“Dr. Han”) and other research scientists. Biosuccess uses its confidential,
28 proprietary, and trade-secret information for, among other things, submissions to the

1 U.S. Food and Drug Administration (“FDA”), and as a basis for filing both domestic
2 and foreign patent applications. Neither Biosuccess’s trade secrets nor its
3 confidential and proprietary information are public or generally known.

4 18. Biosuccess’s trade-secret information is contained in various
5 documents and electronic files. Biosuccess takes great care to maintain the secrecy
6 of its trade-secret and other confidential and proprietary information, and to prevent
7 their disclosure to persons outside the Company, including requiring employees to
8 sign a non-disclosure agreement and abide by the Employee Handbook.

9 19. Based on Biosuccess’s trade secret and other confidential and
10 proprietary information, Biosuccess has been involved with two clinical studies.
11 The first is NCT01009931, titled “Phase II Study of TPA Plus Dexamethasone &
12 CMT in Hematologic Malignancies.” The second is NCT01795924, titled “Safety
13 and Efficacy Study of PD-616 Plus Cytarabine to Treat Acute Myelogenous
14 Leukemia or Myelodysplastic Syndrome (AML/MDS),” which has two trial sites –
15 at the City of Hope Comprehensive Cancer Center and University of Kentucky
16 Medical Center.

17 **B. Relevant Employment Agreements**

18 20. During all relevant times (around August 2006 to January 2013), third
19 party Richard Chang was a shareholder, officer, employee, and a member of the
20 Board of Directors of Biosuccess. Although Richard Chang did not contribute or
21 participate with respect to Biosuccess’s trade-secret and other confidential and
22 proprietary information, he had knowledge and access to all of Biosuccess’s most
23 sensitive information, including years of research data related to PD-616 and its
24 proprietary formulations and treatment applications.

25 21. Defendant Ben Chang is the son of Richard Chang. In 2006, Ben
26 Chang became a consultant for Biosuccess. Ben Chang’s role was as Biosuccess’s
27 Chief Finance Officer, Chief Operating Officer and President for the North America
28 operation. In his role, Ben Chang had knowledge and access to all of Biosuccess’s

1 most sensitive information, including years of research data related to PD-616 and
2 its proprietary formulations and treatment applications.

3 22. As a condition of their employment, Richard Chang and Ben Chang
4 were obligated to protect Biosuccess's trade secret and other confidential and
5 proprietary business information. For instance, Biosuccess's Employee Handbook
6 provides, in pertinent part, that:

7 a. The information protected includes, among other things, "new
8 product research, pending projects and proposals, proprietary production processes,
9 research and development strategies, [and] scientific data."

10 b. Employees agreed that they would "only share such information
11 with those individuals who have authorized access with prior written approval, from
12 Biosuccess' Chief Financial Officer."

13 c. Employees agreed that upon termination of employment that
14 they must return all Biosuccess property.

15 23. On or around January 1, 2013, Ben Chang was asked by Biosuccess to
16 turn in his work related computer provided by Biosuccess and to preserve all
17 information, including any emails. Ben Chang failed to cooperate and instead
18 erased the entire contents of his work related computer, including deleting all
19 emails.

20 24. During his employment as Biosuccess's consultant and officer,
21 Defendant Ben Chang, accessed and gathered for his own unauthorized purposes
22 most, if not all, of Biosuccess's trade-secret and other confidential and proprietary
23 information, including research data related to PD-616 and its proprietary
24 formulations and treatment applications. Defendant Ben Chang then
25 misappropriated Biosuccess's trade-secret information and transferred and took its
26 other confidential and proprietary information in violation of his obligations and
27 without Biosuccess's knowledge, permission, or authorization.

28 25. On information and belief, Richard Chang, Ben Chang, and other

1 unknown Doe Defendants conspired together to steal Biosuccess's most sensitive
2 information for their own benefit and against Biosuccess's interests.

3
4 **C. Defendants Conspired to Destroy Biosuccess by Stealing and Using
Biosuccess's Intellectual Property and Confidential Information**

5 26. Upon information and belief, beginning in 2012 and continuing through
6 today, Richard Chang, Ben Chang, and other unknown Doe Defendants conspired to
7 destroy Biosuccess through unethical and outrageous behavior, including spreading
8 untrue and misleading statements to the employees of the U.S. Subsidiary regarding
9 the financial state of the company, and disclosed to others trade secrets and other
10 confidential and proprietary business information, including the company's payroll
11 information. They also made repeated attempts to induce Dr. Han to take his
12 research and data and defect with them to outside investors, by offering Dr. Han
13 millions of dollars in return.

14 27. Without authorization, Defendant Ben Chang registered himself as a
15 managing member of Biosuccess's U.S. subsidiary.

16 28. Upon information and belief, in furtherance of the conspiracy and plan
17 to destroy Biosuccess, Ben Chang approached and brought in Nepia, and
18 orchestrated a plan to misappropriate Biosuccess's trade secret and confidential and
19 proprietary information. On or around July 18, 2013, according to Nepia's S.E.C.
20 filings, Nepia entered into a Memorandum of Understanding and Asset Assignment
21 Agreement with Defendant Imagic and Defendant RLC Holdings to acquire certain
22 alleged assets including United States Patent No. 6,063,814, entitled "Phorbol esters
23 as anti-neoplastic and white blood cell elevating agents" (the "'814 Patent") and all
24 related intellectual property associated with the patent. According to the SEC
25 filings, cash and stock were exchanged in return.

26 29. On July 18, 2013, Nepia appointed Ben Chang as its President, Chief
27 Executive Officer, Chief Financial Officer, Secretary, Treasurer and Director.
28

1 30. Nepia represented in its S.E.C. filings that “[u]nder the direction of our
2 newly appointed officer and director . . . we intend to pursue the development of
3 PD-616 (12-O-tetradecanoylphorbol-13-acetate) for the treatment of: Acute
4 Myelogenous Leukemia (“AML”) and Stroke (for the treatment of loss of function
5 cause by Stroke)”

6 31. Nepia stated in its S.E.C. filings that “The priority drug development
7 efforts of the Company are focused on the use of PD-616, a naturally occurring
8 compound that has a number of properties that are uniquely suited for the treatment
9 of patients with Acute Myelocytic Leukemia (AML). Company scientists had
10 worked with PD-616 in the laboratory for many years studying its ability to convert
11 cancer cells to normal cells, a process called differentiation. It was also observed in
12 some instances to cause cancer cell death. These observations were the basis of the
13 proposal to test PD-616 in relapsed AML patients in China and later in the US and
14 resulted in findings that were sufficiently encouraging to support further interest in
15 this drug to treat.”

16 32. In fact, Nepia has performed none of the drug development or work
17 stated in the aforesaid S.E.C. filings. Instead, the drug development and clinical
18 work involving PD-616 and its treatment of AML was a result of work funded and
19 performed by Biosuccess. PD-616 is the unique name created by Biosuccess for its
20 TPA drug and Biosuccess’s proprietary property.

21 33. On or around August 12, 2013, third party Richard Chang recorded
22 with the United States Patent and Trademark Office (“USPTO”) an assignment of
23 the ‘814 Patent and United States Patent Application Nos. 13/745,745 (the “‘745
24 patent application”) and 13/745,740 (the “‘740 patent application”) to RLC
25 Holdings. The contact person and correspondence address for the assignment is his
26 son, Defendant Ben Chang, 312 North Mansfield Avenue, Los Angeles, California
27 90036. Richard Chang also appointed a Power of Attorney to Ben Chang.

28 34. In fact, in 2006, Dr. Han and Richard Chang, who are the named

1 inventors, had already assigned all rights under the '814 Patent to Biosuccess by an
2 agreement titled, "Assignment of Patent Right & Assignment of Right of Patent
3 Application Agreement." Said assignment agreement was first recorded on
4 November 14, 2006.

5 35. The '814 Patent recites 20 claims – 2 independent claims and 18
6 dependent claims. Claim 1 covers the method of treating leukemia (which includes
7 AML) using TPA. Claim 11 covers the pharmaceutical composition of TPA.

8 36. Richard Chang is no longer a named inventor on the '745 patent
9 application or the '740 patent application. Hence, Richard Chang's attempts to
10 assign the patent applications are invalid or void.

11 37. On or around September 3, 2013, Nepia changed its name to Rich
12 Pharmaceuticals, Inc. (although the Changs were already using the Rich
13 Pharmaceuticals entity name elsewhere for many years).

14 38. In late 2013, Defendant Ben Chang, his father Richard Chang and Rich
15 Pharmaceuticals engaged a third party Contract Research Organization, Theragene
16 dba Therinova Development ("Theragene" or "Therinova"). Therinova was to
17 provide "regulatory support to include the development of the US FDA IND
18 Submission Package for Rich Pharmaceuticals's product PD-616." The contact
19 person at Theragene was its CEO Jon Berglin.

20 39. Therinova's "deliverables" included "Prior data and documentation
21 review: [] Therinova will review all prior regulatory documentation, research data,
22 and manufacturing information provided by Rich Pharmaceuticals."

23 40. Therinova's scope of work was based on the following assumptions:
24 "At the start of this project, the Company will provide to Therinova the following
25 information: 1. Copy of all Regulatory Correspondence and documentation. 2. All
26 Data pertaining to the pre-clinical and clinical development of PD-616. 3. All
27 information pertaining to the manufacture of PD-616. 4. All additional information
28 needed directly for the US FDA IND Submission."

1 41. As John Berglin attested, Defendant Ben Chang and his father Richard
2 Chang did in fact provide to Therinova numerous confidential Biosuccess
3 documents that they had unlawfully retained. The Declaration of John Berglin is
4 attached as **Exhibit D**. Defendant Ben Chang and his father Richard Chang were
5 instrumental in the creation of Rich Pharmaceuticals, a company in direct
6 competition with Biosuccess.

7 42. Defendant Ben Chang and his father Richard Chang intentionally took
8 Biosuccess documents without authorization. They added the Rich
9 Pharmaceuticals' logo, and inserted untrue and inaccurate language to the effect that
10 Rich Pharmaceuticals was in partnership or working with Biosuccess, in order to
11 benefit from the many years of work of Biosuccess and Dr. Han. The curriculum
12 vitae of both Defendant Ben Chang and Richard Chang, as well as the Rich
13 Pharmaceuticals website, state that Ben Chang and Richard Chang worked for
14 Biosuccess. Thus, a third party would have no reason not to believe these
15 misleading and inaccurate representations by Defendant Ben Chang or Richard
16 Chang.

17 43. On September 6, 2013, Ben Chang entered into an employment
18 agreement with Rich Pharmaceuticals, Inc. as its President, Chief Executive Officer,
19 Chief Financial Officer, and Secretary. Ben Chang was also appointed one of two
20 directors of Rich Pharmaceuticals.

21 44. Upon information and belief, Richard Chang serves as the Chief
22 Scientific Officer and is on the Board of Rich Pharmaceuticals.

23 45. Ben Chang oversaw Biosuccess's entire U.S. operation and was the
24 designated (if not sole) person of contact for most of the operation, from patent
25 filings, financial management and clinical trials. Ben Chang had access to
26 Biosuccess's trade secret and other confidential and proprietary information, and he
27 is using that information in his role as President, Chief Executive Officer, Chief
28 Financial Officer, Secretary and Director at Rich Pharmaceuticals, including

1 conducting clinical trials at two sites in the U.S., meeting with the top ranking
2 foreign health officers, maintaining Rich Pharmaceuticals's patent portfolio, and
3 preparing submissions to the FDA.

4 46. At the direction of Ben Chang, and with the explicit cooperation of
5 third party Richard Chang, Defendants engage in direct competition with
6 Biosuccess, including by making, using, selling, offering to sell within the United
7 States, and/or by importing into the United States, inventions claimed by the '814
8 Patent.

9 47. In July 2013, Defendants contacted WuXi AppTec Co., Ltd. ("WuXi")
10 to manufacture TPA. WuXi is Biosuccess's contract manufacturer of PD-616, and
11 has access to Biosuccess's confidential information. Defendants used the trade
12 secret and confidential information learned and taken from Biosuccess to facilitate
13 the manufacturing of TPA. Upon information and belief, Defendants import TPA
14 produced by WuXi into the United States.

15 48. Upon information and belief, after Defendants import TPA into the
16 United States, Rich Pharmaceuticals and Ben Chang send the TPA to, *inter alia*, Dr.
17 Roger Strair at The Rutgers University for use in clinical studies. Rich
18 Pharmaceuticals and Ben Chang have a close relationship with Dr. Strair. Rich
19 Pharmaceuticals also refers to Dr. Strair on its website as a person to contact for
20 clinical trials and Ben Chang runs the clinical trials for Rich Pharmaceuticals.
21 Richard Chang listed Dr. Strair as a trial witness for the trial in this case that had
22 originally been set for June 17, 2014.

23 49. Defendants, as well as David Chou, a former Biosuccess employee and
24 key contact person with WuXi, participated from manufacturing of the product to its
25 use. David Chou sits on Rich Pharmaceuticals' Board and serves as Rich
26 Pharmaceuticals' CMC Director, the same role he held at Biosuccess.

27 50. Rich Pharmaceuticals' website states under "Legal Grounds" that "Rich
28 Pharmaceuticals is protected by an issued 'use patent' that gives sole rights to the

1 Company to use the intravenous administration of TPA for therapeutic purposes.
2 Since TPA can only be administered for therapeutic purposes by this route, this
3 patent provides complete protection for the use of TPA for any other use.”

4 51. Upon information and belief, the only issued patent to which Rich
5 Pharmaceuticals believes that it has a license is the ‘814 Patent. But, in fact,
6 Biosuccess has been, and still is, the sole assignee and owner of the ‘814 Patent.
7 Biosuccess has not given Rich Pharmaceuticals a license to any “use” rights in the
8 ‘814 Patent.

9 52. Rich Pharmaceuticals is a publicly traded company under the symbol
10 RCHA.

11 53. Contrary to sworn statements made two months ago by its CEO Ben
12 Chang, it now appears that Rich Pharmaceuticals is an active company and just
13 announced successful fundraising from “three accredited investors” of
14 approximately \$400,000 in 2014. Attached as **Exhibit E** to the Complaint is a copy
15 of Rich Pharmaceuticals’ news release dated April 30, 2014. Rich Pharmaceuticals
16 announced plans to hire a Contract Research Organization to prepare filings for the
17 FDA related to AML and “for legal, patent and administrative related expenses.”
18 See **Exhibit E**.

19 **D. Defendants Copy the Biosuccess Website**

20 54. Biosuccess first published its website on or about 2006, and applied for
21 a copyright registration in 2013.

22 55. On information and belief, starting around 2011, a web designer named
23 Ben Alamilla began copying the Biosuccess website, *verbatim*, without
24 Biosuccess’s knowledge or authorization, at the direction of Defendants. Ben
25 Alamilla is the same web designer who had been hired to create the Biosuccess
26 website.

27 56. On information and belief, on or around October 18, 2013, Rich
28 Pharmaceuticals published its website at www.richpharmaceuticals.com. Upon

reviewing the website, it became immediately obvious that Defendants had wholesale copied large portions of Biosuccess's website. For example, the Rich Pharmaceuticals "About Us" webpage is copied nearly verbatim from the Biosuccess "About Us" webpage. True and correct copies of the screenshots of Rich Pharmaceuticals "About Us" webpage and Biosuccess "About Us" webpage are attached as **Exhibit A** to this Complaint. Upon further investigation, Biosuccess discovered that Rich Pharmaceuticals had used the Biosuccess website as a "template" for creating the Rich Pharmaceuticals website. A true and correct copy of the screenshot of Rich Pharmaceuticals "About Us" by Ben Alamilla is attached as **Exhibit B** to this Complaint.

57. As the chart below shows, Rich Pharmaceuticals's website is verbatim or nearly identical to Biosuccess's website in many key aspects:

<u>Page Description</u>	<u>Biosuccess Website</u>	<u>Rich Pharmaceuticals Website</u>
About Us	About Us Founded in 2005, Biosuccess Biotech Co. Ltd. is a privately held company. It focuses on the development of PD-616 (12-O-tetradecanoylphorbol-13-acetate, also known as TPA) for the treatment of AML and AIDS/HIV. <u>The work of two scientists, Prof. Richard Chang & Prof. Zhang Tao Han sustained by their knowledge of this agent's characteristics and their wide experience of years is the basis for the company's interest in using PD-616 in treatment.</u>	About Us Rich Pharmaceuticals is a biopharmaceutical company that became a public entity August 26, 2012 as a result of a reverse merger with Nepia Inc. The Company is focused on the development of its lead product, TPA (12-O-tetradecanoylphorbol-13-acetate), for the treatment of acute myelogenous leukemia (AML) in refractory patients, and the reversal of physical disabilities resulting from stroke. The basis for the interest of the Company to pursue clinical development of TPA in these and possibly other indications is the <u>result</u>

1		<u>of the work of two scientists, Prof. Richard Chang and Prof. Zhang Tao Han. Both have conducted research on TPA for many years and have become experts in the characteristics of this molecule. Their findings form the scientific basis for the clinical use of TPA.</u>
2	About Us	AML Studies with TPA (PD-616) <u>Clinical studies were conducted in China in patients who had few (sometimes none) remaining options for therapy in acute myelogenous leukemia (AML).</u>
3		AML Studies with TPA <u>Initially, clinical studies were conducted in leading hospitals in China in patients who had few, if any, options remaining for the treatment AML.</u>
4	About Us	AML Studies with TPA (PD-616) <u>These patients were refractory to standard therapy and had debilitating symptoms.</u>
5		AML Studies with TPA <u>These patients were refractory to standard therapy and had debilitating symptoms that were life threatening.</u>
6	About Us	AML Studies with TPA (PD-616) <u>Findings showed that some patients were put into partial remission and established the short term safety for the intravenous administration of PD-616.</u>
7		AML Studies with TPA <u>The clinical status of some of the patients treated with TPA changed favorably to partial remission. In addition, the short term safety of TPA was established in these individuals using an intravenous formulation of TPA.</u>
8	About Us	AML Studies with TPA (PD-616) <u>Encouraged by the clinical results from China, Roger Strair MD, PhD, a leading oncologist at The Cancer Institute of New Jersey (CINJ), at the University of Medicine and Dentistry of N.J.</u>
9		AML Studies with TPA <u>Encouraged by the clinical results with TPA in China, Roger Strair MD, PhD, a leading oncologist at the University of Medicine and Dentistry at Rutgers University, obtained an</u>

	(UMDNJ), <u>obtained an investigator IND</u> , and conducted a Phase 1 study in patients the majority of whom also had <u>relapsed/refractory AML</u> .	<u>investigator IND</u> and successfully completed a Phase 1 study in patients, the majority of whom had <u>relapsed/refractory AML</u> .
About Us	AML Studies with TPA (PD-616) Based on Phase 1 findings, Biosuccess Biotech was <u>encouraged by Dr. Strair to conduct a Phase 2 study in relapsed/refractory AML</u> .	AML Studies with TPA Rich Pharmaceuticals was <u>encouraged by Dr. Strair to conduct a Phase 2 study in relapsed/refractory AML</u> .
About Us	AML Studies with TPA (PD-616) <u>Currently, a Phase 2 study is underway and the recruitment of refractory AML patients is actively done by Dr. Strair.</u>	AML Studies with TPA <u>A Phase 2 study is currently underway under the direction of Dr. Strair who is actively enrolling appropriate patients in this study.</u>
About Us- Legal Grounds	Legal Grounds <u>Biosuccess Biotech is protected by an issued "use patent" that provides sole rights to use the intravenous administration of PD-616 for therapeutic purposes (2001).</u>	Legal Grounds <u>Rich Pharmaceuticals is protected by an issued "use patent" that gives sole rights to the Company to use the intravenous administration of TPA for therapeutic purposes.</u>
Technology	Technology <u>Biosuccess Biotech Co. Ltd. pursues the development of TPA (12-O-tetradecanoylphorbol-13-acetate) for the treatment of AML and HIV/AIDS. TPA is often referred to as PD-616 or PMA (phorbol 12-myristate-13-acetate).</u>	Our Science <u>Rich Pharmaceuticals currently is focused on the clinical development of the chemical molecule TPA (12-O-tetradecanoylphorbol-13-acetate) for the treatment of acute myelogenous leukemia (AML).</u>
Technology	PD-616 <u>PD-616 has been widely studied for characteristics that are unique to this chemical class among which are a potent ability to</u>	TPA <u>TPA has characteristics that are unique to this chemical class including a potent ability to accelerate differentiation of</u>

	<u>accelerate differentiation of the myeloid cell lines, HL-60 and THP-1, as well as mononuclear phagocytes from bone marrow and peripheral blood.</u>	<u>the myeloid cell lines, HL-60 and THP-1, as well as mononuclear phagocytes from bone marrow and peripheral blood.</u>
Technology	PD-616 <u>The best characterized receptor for PD-616 is protein kinase C (PKC) which, once activated, induces substrate phosphorylation that propagates signals to MAPK cascades.</u>	TPA <u>The best characterized receptor for TPA is protein kinase C (PKC) which, once activated, induces substrate phosphorylation that propagates signals to the MAPK cascades.</u>
Technology	PD-616 <u>The effect of PD-616 on MAPK pathways may be particularly relevant to the differentiating and pro-apoptotic effects of PD-616 in certain cells.</u>	TPA <u>The effects of TPA on MAPK pathways may be particularly relevant to the differentiating and pro-apoptotic effects of TPA in certain cells.</u>
Technology	PD-616 <u>The capacity of PD-616 to activate PKC and to induce phenotypic changes characteristic of differentiation and/or apoptosis led investigators to study its effect in AML and HIV/AIDS.</u>	TPA <u>The capacity of TPA to activate PKC and to induce phenotypic changes characteristic of differentiation and/or apoptosis led investigators to study its effect in AML.</u>

FIRST CAUSE OF ACTION

(Patent Infringement)

Against Rich Pharmaceuticals, Ben Chang, Imagic LLC,

Richard L. Chang Holding LLC and DOES 1-10

58. Biosuccess incorporates by reference the paragraphs above as if fully set forth herein.

1 59. On May 21, 2000, the ‘814 Patent was issued by the USPTO. A true
2 and correct copy of the ‘814 Patent is attached as **Exhibit C** to this Complaint.

3 60. Biosuccess is the assignee and owner of the right, title and interest in
4 and to the ‘814 Patent, including the right to assert all causes of action arising under
5 said patent and the right to any remedies for infringement of it.

6 61. In violation of 35 U.S.C. § 271, Defendants have directly infringed and
7 continue to directly infringe, literally and/or under the doctrine of equivalents, the
8 ‘814 Patent by making, using, selling, offering to sell within the United States,
9 and/or importing into the United States, including in this Judicial District, inventions
10 claimed by the ‘814 Patent (“the ‘814 Accused Products and Uses”), without
11 authority from Biosuccess.

12 62. The ‘814 Accused Products and Uses, include, but are not limited to,
13 pharmaceutical compositions of TPA and the use of TPA for treating patients with
14 leukemia.

15 63. Defendants have had actual knowledge of the ‘814 Patent since it was
16 filed with the USPTO, and of its infringement since at least July 18, 2013, when
17 Nepia entered into a Memorandum of Understanding and Asset Assignment
18 Agreement with Defendant Imagic and Defendant RLC Holdings to purportedly
19 acquire certain assets including the ‘814 Patent and all related intellectual property
20 associated with the patent.

21 64. Upon information and belief, Defendants Rich Pharmaceuticals and
22 Ben Chang have committed and continue to commit acts of contributory
23 infringement of at least claim 1 (the method of treating leukemia (which includes
24 AML) using TPA) of the ‘814 Patent under 35 U.S.C. §271(c) by selling, offering to
25 sell, and/or importing materials for use (including, *inter alia*, providing TPA to
26 entities such as Dr. Roger Strair for use in clinical studies), knowing or willfully
27 blind to the fact that these material and use constitute a material part of the
28 invention, were especially made or especially adapted for use in infringing the ‘814

1 Patent, and have no substantial non-infringing uses.

2 65. Upon information and belief, Defendants Rich Pharmaceuticals and
 3 Ben Chang have induced and continue to induce others to infringe the '814 Patent
 4 under 35 U.S.C. § 271(b) by, among other things, and with specific intent, actively
 5 and knowingly aiding and abetting others to infringe, including, but not limited to,
 6 those who use products or perform the methods claimed in the '814 Patent that
 7 constitutes direct infringement of the '814 Patent (at least claim 1), including, *inter*
 8 *alia*, Dr. Roger Strair. On information and belief, Defendant engaged in such
 9 actions with specific intent to cause infringement or with willful blindness to the
 10 resulting infringement because Defendants have had actual knowledge of the '814
 11 Patent and that its acts were inducing others to infringe the '814 Patent.

12 66. As a result of Defendants' direct and indirect infringement of the '814
 13 Patent, Biosuccess has suffered both monetary damages and other damages that
 14 cannot be compensated by monetary means. Biosuccess will continue to suffer
 15 damages in the future unless Defendants' infringing activities are enjoined by this
 16 Court.

17 67. Unless a permanent injunction is issued enjoining Defendants from
 18 infringing the '814 Patent, Biosuccess will be greatly and irreparably harmed.

19 **SECOND CAUSE OF ACTION**

20 **(Copyright Infringement)**

21 **Against Rich Pharmaceuticals, Ben Chang, and Does 1-10**

22 68. Biosuccess incorporates by reference the paragraphs above as if fully
 23 set forth herein.

24 69. Rich Pharmaceuticals is infringing Biosuccess's copyrighted website in
 25 violation of the Copyright Act by its wholesale copying and re-publishing of
 26 Biosuccess's website on its www.richpharmaceuticals.com website. The Rich
 27 Pharmaceuticals website is substantially similar, if not identical, to Biosuccess's
 28 own website.

1 70. On information and belief, Defendants' infringement has been
2 deliberate, willful, malicious, oppressive, and without regard to Biosuccess's
3 proprietary rights.

4 71. On information and belief, Defendant Ben Chang has been personally
5 involved in directing and causing Rich Pharmaceuticals to engage in its copyright
6 infringement of Biosuccess's website.

7 72. Defendants' copying of the Biosuccess website without Biosuccess's
8 authority or consent and is also in violation of the Employee Handbook, and is in
9 willful and conscious disregard of Biosuccess's rights under the federal Copyright
10 Act.

11 73. Defendants' copyright infringement has caused, and will continue to
12 cause, Biosuccess to suffer substantial injuries, loss, and damage to its proprietary
13 and exclusive rights and has further damaged Biosuccess's business reputation and
14 goodwill, diverted its trade, and caused loss of profits, all in an amount to be
15 determined. In addition, Plaintiff Biosuccess is entitled to receive the profits made
16 by Defendants from their wrongful acts pursuant to 17 U.S.C. Section 504.

17 74. In infringing Biosuccess's copyright interests, Defendants acted
18 willfully and maliciously, entitling Biosuccess to enhancement of any statutory
19 damages, pursuant to 17 U.S.C. § 504(c)(2), in an amount to be determined at trial.

20 75. Defendants' copyright infringement and the threat of continuing
21 infringement has caused and will continue to cause Biosuccess repeated and
22 irreparable injury. It would be difficult to ascertain the amount of money damages
23 that would afford Biosuccess adequate relief at law for Defendants' acts and
24 continuing acts. Plaintiff's remedy at law is not adequate to compensate it for the
25 injuries already inflicted and further threatened by Defendants. Therefore, Plaintiff
26 is entitled to preliminary and permanent injunctive relief pursuant to 17 U.S.C.
27 Section 502.

28 76. As a direct and proximate result of Defendants' willful infringement of

1 Biosuccess's copyright interests, Biosuccess has had to retain legal counsel, and it is
 2 entitled to recover its attorneys' fees from Defendants pursuant to 17 U.S.C. § 505,
 3 as well as costs, including any expert fees that might be appropriately recoverable.

4 5 **THIRD CAUSE OF ACTION**

6 **(Misappropriation of Trade Secrets – Cal. Civ. Code § 3426.1 et seq.)**

7 **Against All Defendants**

8 77. Biosuccess incorporates by reference the paragraphs above as if fully
 9 set forth herein.

10 78. Biosuccess is informed and believes, and on that basis alleges, that
 11 Defendants acquired Biosuccess's valuable trade secrets for unauthorized purposes
 12 and are using Biosuccess's trade secrets, without Biosuccess's consent, to
 13 unlawfully compete against Biosuccess.

14 79. Biosuccess enjoys an advantage over its existing and would-be-
 15 competitors based, in part, on the trade-secret information it has developed and
 16 implemented in its effort to bring PD-616 to market for the treatment of, among
 17 other diseases, leukemia, and stroke.

18 80. Biosuccess has made reasonable efforts under the circumstances to
 19 preserve the confidentiality of its trade secrets. Such information derives
 20 independent economic value (actual and potential) from not being generally known
 21 to the public or to other persons who can obtain economic value from its disclosure
 22 or use. Accordingly, such information constitutes "trade secrets" under California's
 23 UTSA, Cal. Civ. Code Section 3426 *et seq.*

24 81. Defendants were and remain under a duty not to use or disclose
 25 Biosuccess's trade secrets other than for the benefit of Biosuccess and only with
 26 Biosuccess's authorization. By taking or using this information from Biosuccess
 27 without its authorization, Defendants knew that they acquired such information
 28 under circumstances giving rise to a breach of a duty to maintain its secrecy and

1 limit its use.

2 82. Defendants' conduct constitutes misappropriation of Biosuccess's trade
3 secrets through the unauthorized taking, retention and use of Biosuccess's trade
4 secret information.

5 83. Defendants' actual and threatened misappropriation was and is being
6 carried out without the express or implied consent of Biosuccess.

7 84. On information and belief, Defendants obtained Biosuccess's trade
8 secret information from Biosuccess and not from generally available information or
9 through their own independent research and efforts.

10 85. The actions of Defendants constitute willful misappropriation and/or
11 threatened misappropriation of Biosuccess's trade secrets under the California's
12 UTSA, Cal. Civ. Code Section 3426 *et seq.*

13 86. As a direct and proximate result of Defendants' conduct, Defendants
14 have been unjustly enriched in an amount to be ascertained at trial, and Biosuccess
15 has sustained, and will continue to sustain, actual damages in an amount to be
16 proven at trial.

17 87. Defendants' actual and threatened misappropriation of Biosuccess's
18 trade secrets, unless and until enjoined and restrained by order of this Court, is
19 causing and will continue to cause great and irreparable harm to Biosuccess.
20 Biosuccess is threatened with losing its intellectual property, as well current and
21 potential business and investors.

22 88. Pursuant to California Civil Code section 3426.2, Biosuccess is entitled
23 to an injunction to prohibit Defendants from using, disclosing or otherwise
24 benefiting from Biosuccess's trade secrets, to eliminate any commercial advantage
25 to Defendants that they may otherwise derive from their misappropriation, and to
26 require Defendants to immediately return to Biosuccess all information, equipment
27 and other materials which they have wrongfully obtained.

28 89. In performing the conduct described herein, Defendants acted willfully

1 and maliciously with the intent to injure Biosuccess and to wrongfully advantage
2 themselves at Biosuccess's expense.

3 90. Pursuant to California Civil Code section 3426.3(c), Biosuccess is
4 entitled to an award of punitive and exemplary damages against Defendants, and
5 each of them, sufficient to punish and deter them from engaging in such conduct in
6 the future, in an amount to be ascertained at trial.

7 91. Pursuant to California Civil Code section 3426.4, Biosuccess is also
8 entitled to an award of their attorneys' fees and costs incurred in this action.

9 10 **FOURTH CAUSE OF ACTION**

11 **(Breach of Fiduciary Duty)**

12 **Against Ben Chang**

13 92. Biosuccess incorporates by reference the paragraphs above as if fully
14 set forth herein.

15 93. As an officer of Biosuccess, Ben Chang owed fiduciary duties to
16 Biosuccess, including a duty of loyalty.

17 94. In reliance on such duties, Biosuccess entrusted Ben Chang with
18 maintaining confidential and proprietary information as well as with overseeing
19 certain special projects. Biosuccess reposed confidence in Ben Chang that he would
20 maintain his duties and not disclose its confidential or proprietary information or use
21 it for his own personal gain.

22 95. Ben Chang knowingly and intentionally breached his fiduciary duties to
23 Biosuccess by the actions described above, including by conveying Biosuccess's
24 confidential and proprietary information to third parties, including Rich
25 Pharmaceuticals and Theragene; by using such information without Biosuccess's
26 consent and by causing and encouraging third parties to do so; and by using them
27 for his own personal gain, to Biosuccess's detriment.

28 96. As a direct and proximate result of Ben Chang's breach of his fiduciary

1 duties, Biosuccess has suffered, and will continue to suffer, substantial monetary
2 damages in an amount to be proven at trial.

3 97. Ben Chang and through others also made repeated attempts to induce
4 and pressure Dr. Han, another Director, Officer and key Biosuccess scientist, to
5 leave Biosuccess by offering Dr. Han millions of dollars.

6 98. Ben Chang is guilty of oppression, fraud, and malice regarding the
7 breaches of his fiduciary duties, acting not only to benefit him and third parties, but
8 with the intent and result of causing injury to Biosuccess and with a willful and
9 conscious disregard for Biosuccess's rights. Ben Chang intentionally
10 misrepresented, concealed, and deceived Biosuccess regarding material facts with
11 the intention of injuring Biosuccess and depriving it of its valuable confidential and
12 proprietary information. Biosuccess is entitled to an award of punitive and
13 exemplary damages against Ben Chang sufficient to punish and deter him from
14 engaging in such conduct in the future, in an amount to be ascertained at trial.

15 **FIFTH CAUSE OF ACTION**

16 **(Unfair Competition Pursuant to California Business and Professions Code**

17 **Section 17200, et seq.)**

18 **Against All Defendants**

19 99. Biosuccess incorporates by reference the paragraphs above as if fully
20 set forth herein.

21 100. The above-described conduct of the Defendants constitutes unlawful
22 and unfair business practices in violation of California Business and Professions
23 Code Section 17200, *et seq.*

24 101. Defendants' unlawful business practices include, without limitation,
25 Defendants' infringement of Biosuccess's patent and copyright interests,
26 misappropriation of non-trade-secret confidential and proprietary information, acts
27 of conversion, breaches of fiduciary duty, misrepresenting that Biosuccess and Rich
28 Pharmaceuticals were in partnership or working together, and other wrongs

1 described herein.

2 102. Defendants have acted deliberately with the intent to unfairly benefit
3 from the expense, time, effort and labor expended by Biosuccess in the research and
4 development of PD-616 and its intellectual property related thereto, and with a
5 callous disregard for Biosuccess's rights.

6 103. Pursuant to California Business and Professions Code Section 17203,
7 Defendants are required to restore to Biosuccess all property acquired by means of
8 Defendants' unfair competition with Biosuccess.

9 104. As a result of Defendants' conduct, Defendants have been or will be
10 unjustly enriched in an amount to be proven at trial, for which Biosuccess seeks
11 restitution.

12 105. As a result of the actions of Defendants, Biosuccess has suffered and
13 will continue to suffer irreparable harm unless and those unlawful business practices
14 will continue to cause such irreparable harm until Defendants' conduct is enjoined.

15 16 **SIXTH CAUSE OF ACTION**

17 **(Unfair Competition under California Common Law)**

18 **Against All Defendants**

19 106. Biosuccess incorporates by reference the paragraphs above as if fully
20 set forth herein.

21 107. The above-described conduct of the Defendants constitutes unfair
22 competition under the common law of the State of California.

23 108. Because Defendants' conduct has been intentional and willful and in
24 conscious disregard of the rights of Biosuccess, Biosuccess is entitled to punitive
25 damages against Defendants.

26 **SEVENTH CAUSE OF ACTION**

27 **(Violation of Cal. Pen. Code § 502)**

28 **Against Ben Chang**

109. Biosuccess incorporates by reference the paragraphs above as if fully set forth herein.

110. Cal. Pen. Code §502(c) prohibits an individual from knowingly accessing and without permission altering, damaging, deleting, destroying, disrupting, or otherwise using a computer system or computer network. It also prohibits an individual from assisting or providing a means to violate §502(a).

111. As alleged above, before he was terminated, Ben Chang destroyed and erased all of the computer files in the Biosuccess system related to the U.S. operations.

112. Biosuccess is continuing to spend money to investigate the extent of damage caused by Ben Chang's malicious actions, to verify the Biosuccess's information system was or was not otherwise altered and the extent of the information deleted and/or destroyed by Ben Chang.

113. Biosuccess has suffered and will continue to suffer injury to its business, including but not limited to its computer system. Pursuant to Cal. Pen. Code §502(e), Biosuccess seeks injunctive relief, compensatory damages, attorneys' fees, and punitive or exemplary damages.

EIGHTH CAUSE OF ACTION

(Trespass to Chattels)

Against Ben Chang

114. Biosuccess incorporates by reference the paragraphs above as if fully set forth herein.

115. Biosuccess owns computers in its system network, including the computer assigned to Ben Chang before he was terminated in January 2013.

116. The files on Biosuccess's internal system network, as well as the files on the hard disk drive of the computer assigned to Ben Chang before he was terminated in January 2013, are comprised of data files which Biosuccess possessed

1 and/or had a right to possess.

2 117. Ben Chang intentionally and without authorization interfered with
3 Biosuccess's possessory interest in said computers on the Biosuccess system
4 network, as well as the files on the Biosuccess system network, and the files on the
5 hard disk drives. Prior to his departure from Biosuccess and without authorization,
6 Ben Chang deleted files from the laptop that had been assigned to her by Biosuccess
7 so that the files were not recoverable.

8 118. Ben Chang's unauthorized and malicious actions proximately resulted
9 in damages to Biosuccess.

10 11 **NINTH CAUSE OF ACTION**

12 **(Inducing Breach of Contract)**

13 **Against Rich Pharmaceuticals, Imagic, and RLC Holdings**

14 119. Biosuccess incorporates by reference the paragraphs above as if fully
15 set forth herein.

16 120. On information and belief, third party Richard Chang and Ben Chang
17 signed valid and binding non-disclosure agreements prohibiting those individuals
18 from, among other things, disclosing or exploiting the confidential and proprietary
19 information they learned while working at Biosuccess.

20 121. Biosuccess is informed and believes, and on that basis alleges, that
21 Rich Pharmaceuticals, Imagic, and RLC Holdings knew of the existence of these
22 non-disclosure agreements because, among other things, they are customary in the
23 industry and they use similar non-disclosure agreements in connection with their
24 own research and development.

25 122. Biosuccess is informed and believes, and on that basis alleges, that
26 Rich Pharmaceuticals, Imagic, and RLC Holdings intended to cause, and in fact
27 caused, these individuals to breach these non-disclosure agreements by encouraging
28 them to disclose Biosuccess's confidential and proprietary information and methods.

123. Moreover, Biosuccess is informed and believes, and on that basis alleges, that Rich Pharmaceuticals, Imagic, and RLC Holdings knew that their actions would induce a breach of contract, because, in practical terms, it is impossible for the individuals to research and develop PD-616 without breaching their contractual obligations not to disclose or utilizing protected information.

124. As a direct and proximate result of Rich Pharmaceuticals, Imagic, and RLC Holdings inducing these individuals to breach their non-disclosure agreements, Biosuccess has been damaged in an amount to be proved at trial.

125. This knowing and purposeful disregard for Biosuccess's rights under the non-disclosure agreements is oppressive and malicious. Biosuccess is informed and believes, and on that basis alleges, that officers, directors, or managing agents of Rich Pharmaceuticals, Imagic, and RLC Holdings had advance knowledge of these oppressive and malicious acts and consciously disregarded them or authorized, ratified, or perpetrated the oppressive and malicious acts themselves. As a result of such conduct, Biosuccess is entitled to punitive damages pursuant to California Civil Code § 3294 in an amount to be proved at trial.

TENTH CAUSE OF ACTION

(Inducing Breach of Fiduciary Duty)

Against Rich Pharmaceuticals, Imagic LLC, and RLC Holdings

126. Biosuccess repeats and incorporates by reference the allegations in the paragraphs above, as if fully set forth herein.

127. By virtue of their non-disclosure agreements, their status as officers, and the trust and confidence Biosuccess reposed in them in entrusting its confidential and proprietary information to them, third party Richard Chang and Ben Chang owed Biosuccess a fiduciary duty not to disclose the confidential and proprietary information they learned while working at Biosuccess.

128. Biosuccess is informed and believes, and on that basis alleges, that

1 Rich Pharmaceuticals, Imagic, and RLC Holdings knew of the existence of the non-
2 disclosure agreements and of the fiduciary duties owed to Biosuccess.

3 129. Biosuccess is informed and believes, and on that basis alleges, that in
4 connection with the research and development of PD-616 at Rich Pharmaceuticals,
5 Rich Pharmaceuticals, Imagic, and RLC Holdings intended to cause, and in fact
6 caused, these individuals to breach this fiduciary duty by encouraging them to
7 disclose Biosuccess's confidential and proprietary information to Rich
8 Pharmaceuticals, Imagic, and RLC Holdings.

9 130. Biosuccess is informed and believes, and on that basis alleges, that
10 Rich Pharmaceuticals, Imagic, and RLC Holdings knew that their actions would
11 induce a breach of these individuals' fiduciary duties, because, in practical terms, it
12 is impossible for them to research, develop, and produce PD-616 without breaching
13 their fiduciary duty not to disclose or utilizing protected information.

14 131. As a direct and proximate result of Rich Pharmaceuticals, Imagic, and
15 RLC Holdings inducing third party Richard Chang and Ben Chang to breach their
16 non-disclosure agreements and fiduciary duties, Biosuccess has been damaged in an
17 amount to be proved at trial.

18 132. This knowing and purposeful disregard for Biosuccess's rights is
19 oppressive and malicious. Biosuccess is informed and believes, and on that basis
20 alleges, that officers, directors, or managing agents of Rich Pharmaceuticals,
21 Imagic, and RLC Holdings either had advance knowledge of these oppressive and
22 malicious acts and consciously disregarded them or authorized, ratified, or
23 perpetrated the oppressive and malicious acts themselves. As a result of such
24 conduct, Biosuccess is entitled to punitive damages pursuant to California Civil
25 Code § 3294 in an amount to be proved at trial.

26
27 **ELEVENTH CAUSE OF ACTION**

28 **(For Conversion)**

Against All Defendants

133. Biosuccess repeats and incorporates by reference the allegations in the paragraphs above, as if fully set forth herein.

134. Biosuccess jointly developed and is an owner of the confidential and proprietary information involved with the research and development of PD-616.

135. Biosuccess is informed and believes, and on that basis alleges, that, in the course of working on the research and development of PD-616 in direct competition to Biosuccess, each of the defendants has converted for their own use, Biosuccess's confidential and proprietary information.

136. Biosuccess is entitled to an order that the defendants cease and desist all use and disposition of its confidential and proprietary information in connection with PD-616.

137. As a direct and proximate result of the Defendants' acts of conversion, Biosuccess has suffered damages due to, among other things, the lost value of its confidential and proprietary information.

138. The Defendants' conversion of Biosuccess's property is oppressive and malicious. As a result of such conduct, Biosuccess is entitled to punitive damages pursuant to California Civil Code § 3294 against the defendants in an amount to be proved at trial.

TWELFTH CAUSE OF ACTION

(For Conspiracy)

Against All Defendants

139. Biosuccess repeats and incorporates by reference the allegations in the paragraphs above, as if fully set forth herein.

140. Biosuccess is informed and believes, and on that basis alleges, that, in connection with the Defendants' research and development of PD-616, all Defendants agreed to a common plan to, among other things, infringe Biosuccess's patent and copyright interests, convert Biosuccess's confidential and proprietary

1 information for their own use, and commit the other tortious conduct described in
2 this Complaint.

3 141. Biosuccess is informed and believes, and on that basis alleges, that
4 Defendants had actual knowledge that such tortious conduct would occur and
5 concurred in the scheme with knowledge of its unlawful purpose.

6 142. Biosuccess is informed and believes, and on that basis alleges, that in
7 agreeing to commit such tortious conduct against Biosuccess, Defendants acted for
8 their own individual advantage by disclosing and exploiting Biosuccess's
9 confidential and proprietary information for their own personal gain.

10 143. As a direct and proximate result of Defendants' conspiracy to commit
11 such tortious conduct, Biosuccess has suffered damages in an amount to be proved
12 at trial.

13 144. Defendants' conspiracy to commit tortious conduct against Biosuccess
14 renders each of them liable for all acts taken by their co-conspirators before and
15 after each defendant joined the conspiracy.

16
17 **THIRTEENTH CAUSE OF ACTION**

18 **(For Aiding and Abetting)**

19 **Against All Defendants**

20 145. Biosuccess repeats and incorporates by reference the allegations in the
21 paragraphs above, as if fully set forth herein.

22 146. Biosuccess is informed and believes, and on that basis alleges, that
23 defendants knew disclosure of Biosuccess's confidential and proprietary information
24 would violate non-disclosure agreements and would constitute a breach of fiduciary
25 duties, conversion, misappropriation, and the other wrongs described herein.

26 147. Biosuccess is informed and believes, and on that basis alleges, that in
27 connection with setting up the new companies to research and develop PD-616,
28 defendants gave substantial assistance and encouragement to the other defendants to

1 unlawfully disclose Biosuccess's confidential and proprietary information.

2 148. Biosuccess is informed and believes, and on that basis alleges, that the
3 defendants' mutual assistance and encouragement was a substantial factor causing
4 the disclosure of Biosuccess's confidential and proprietary information and,
5 therefore, was a substantial factor in causing harm to Biosuccess.

6 149. By such conduct, each Defendant aided and abetted the other
7 Defendants in breaching their fiduciary duties to Biosuccess, converting
8 Biosuccess's property for their own use, and committing the other wrongs described
9 herein. All Defendants are therefore jointly responsible for the wrongful conduct of
10 any of the other defendants in this Complaint.

11 12 13 **PRAYER FOR RELIEF**

14 WHEREFORE, BIOSUCCESS prays for the following relief:

15 A. That the Court enters judgment in favor of Biosuccess and against
16 Defendants;

17 B. That the Court determine that Defendants have committed patent and
18 copyright infringement;

19 C. That Defendants, their officers, agents, servants, employees, and all
20 persons in active concert or participation with them, be preliminarily and
21 permanently restrained and enjoined from misappropriating, disclosing, or using
22 Biosuccess's trade secrets and its confidential and proprietary information, and from
23 infringing Biosuccess's patent and copyright interests;

24 E. That Biosuccess recover compensatory damages for Defendants'
25 wrongdoing in an amount to be established at trial, together with pre-judgment and
26 post-judgment interest thereon at the maximum legal rate;

27 G. That Biosuccess recover its proven damages or statutory damages
28 elected in accordance with the Patent Act, 35 U.S.C. §§284 and 285 and the

1 Copyright Act, 17 U.S.C. §§ 504 and 505 and other applicable law.

2 H. That Biosuccess recover an award of punitive and other appropriate
3 exemplary damages, disgorgement, restitution, pre-judgment and post-judgment
4 interest as permitted by statute and/or contract;

5 I. That Biosuccess recover attorneys' fees and the costs of suit herein;

6 J. An award of treble damages under 35 U.S.C. § 284; and

7 K. Such other and further relief as this Court may deem just and proper.

8
9 **DEMAND FOR A JURY TRIAL**

10 Plaintiff Biosuccess hereby demands a jury trial on all issues so triable.

11
12 Dated: May 30, 2014

LEE TRAN LIANG & WANG LLP

13
14 By: /s/ Enoch H. Liang

15 Enoch H. Liang
16 Attorneys for Plaintiff
17 BIOSUCCESS BIOTECH, CO., LTD.
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EXHIBIT A



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About Us

Founded in 2005, Biosuccess Biotech Co. Ltd. is a privately held company. It focuses on the development of PD-616 (12-O-tetradecanoylphorbol-13-acetate, also known as TPA) for the treatment of [AML](#) and [AIDS/HIV](#). The work of two scientists, Prof. Richard Chang & Prof. Zhang Tao Han sustained by their knowledge of this agent's characteristics and their wide experience of years is the basis for the company's interest in using PD-616 in treatment.

AML Studies with TPA (PD-616)

Clinical studies were conducted in China in patients who had few (sometimes none) remaining options for therapy in acute myelogenous leukemia (AML). These patients were refractory to standard therapy and had debilitating symptoms. **Findings showed that some patients were put into partial remission and established the short term safety for the intravenous administration of PD-616.**

Encouraged by the clinical results from China, Roger Strair MD, PhD, a leading oncologist at The Cancer Institute of New Jersey (CINJ), at the University of Medicine and Dentistry of N.J. (UMDNJ), obtained an investigator IND, and conducted a [Phase 1 study](#) in patients the majority of whom also had relapsed/refractory AML. Based on Phase 1 findings, Biosuccess Biotech was encouraged by Dr. Strair to conduct a Phase 2 study in relapsed/refractory AML. Currently, a Phase 2 study is underway and the recruitment of refractory AML patients is actively done by Dr. Strair.

AIDS/HIV Studies with TPA (PD-616)

Three preliminary experiments, part of the clinical research process, were conducted in China on AIDS/HIV. These patients had few treatment options, as they presented many of the injurious effects of this disease and were refractory to standard anti-AIDS drugs. **Following treatment with PD-616, there was a disappearance of symptoms and a return to normal in almost all patients. In the third clinical study, the number of CD4 T-cells was somewhat reduced while the concentration of the virus in blood increased in all patients in 30 days after starting PD-616 treatment, but was almost undetectable at 60 days.** These results are clinical evidence that support the unique mechanism of action proposed for PD-616 in AIDS/HIV. Future clinical studies are needed, but it appears that PD-616 can be a totally new and highly effective drug for the treatment of AIDS. In order to confirm these clinical findings, Biosuccess Biotech Co. Ltd. has plans to conduct rigorously controlled clinical trials in the U.S. during a large Phase 2 study.

Legal Grounds

Biosuccess Biotech is protected by an issued "use patent" that provides sole rights to use the intravenous administration of PD-616 for therapeutic purposes (2001).

A patent application was filed on the use of PD-616 to treat AML in January, 2007. In January, 2008, a patent application was filed for the use of PD-616 in HIV/AIDS and includes coverage of many other phorbol ester structures in the PD-616 chemical class.

Biosuccess Biotech Co. Ltd. has 20 years exclusive rights to the use of PD-616 in AML and HIV/AIDS, beginning with January 30th, 2008.

In June 2011, AML Phase 2 protocol was approved by FDA.

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Medical Professionals

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Patients

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AML Studies

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AIDS Studies

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Latest News

April 27th, 2012

Biosuccess has received an IND approval from the FDA. An Acute Myelocytic Leukemia (AML) study under this IND will be underway shortly.

March 23rd, 2012

A corporate IND has been submitted to the FDA for use of TPA in Acute Myelocytic Leukemia (AML).

June 16th, 2011

Jace Chew joins our team as President of ASEAN, India sub-continent and Australia operations.

June 16th, 2011

AML Phase 2 trial begins recruiting patients.

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[Rich Pharmaceuticals.com](#) » [About Us](#)

About Us

Rich Pharmaceuticals is a biopharmaceutical company that became a public entity August 26, 2012 as a result of a reverse merger with Nepia Inc. The Company is focused on the development of its lead product, TPA (12-O-tetradecanoylphorbol-13-acetate), for the treatment of acute myelogenous leukemia (AML) in refractory patients, and the reversal of physical disabilities resulting from stroke. The basis for the interest of the Company to pursue clinical development of TPA in these and possibly other indications is the result of the work of two scientists, Prof. Richard Chang and Prof. Zhang Tao Han. Both have conducted research on TPA for many years and have become experts in the characteristics of this molecule. Their findings form the scientific basis for the clinical use of TPA.

AML Studies with TPA

Initially, clinical studies were conducted in leading hospitals in China in patients who had few, if any, options remaining for the treatment of AML. These patients were refractory to standard therapy and had debilitating symptoms that were life threatening. The clinical status of some of the patients treated with TPA changed favorably to partial remission. In addition, the short term safety of TPA was established in these individuals using an intravenous formulation of TPA.

Encouraged by the clinical results with TPA in China, Roger Strair MD, PhD, a leading oncologist at the University of Medicine and Dentistry at Rutgers University, obtained an investigator IND and successfully completed a Phase 1 study in patients, the majority of whom had relapsed/refractory AML. Rich Pharmaceuticals was encouraged by Dr. Strair to conduct a Phase 2 study in relapsed/refractory AML. A Phase 2 study is currently underway under the direction of Dr. Strair who is actively enrolling appropriate patients in this study.

Legal Grounds

Rich Pharmaceuticals is protected by an issued "use patent" that gives sole rights to the Company to use the intravenous administration of TPA for therapeutic purposes. Since TPA can only be administered for therapeutic purposes by this route, this patent provides complete protection for the use of TPA for any other use.

About Us

[Company History](#)
[Leadership Team](#)

News

October 2nd, 2013

Rich Pharmaceuticals Inc. has been licensed to pursue the clinical development of their lead drug, TPA, in acute myelogenous leukemia (AML) and stroke.

October 1st, 2013

Rich Pharmaceuticals appoints Robert Thomas as COO

September 6th, 2013

Rich Pharmaceuticals appoints David Chou, PhD. to the Board of Director

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Morbi accumsan convallis est,
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EXHIBIT B



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About Us

Founded in 2005, Biosuccess Biotech Co. Ltd. is a privately held company. It focuses on the development of PD-616 (12-O-tetradecanoylphorbol-13-acetate, also known as TPA) for the treatment of **AML** and **AIDS/HIV**. The work of two scientists, Prof. Richard Chang & Prof. Zhang Tao Han sustained by their knowledge of this agent's characteristics and their wide experience of years is the basis for the company's interest in using PD-616 in treatment.

AML Studies with TPA (PD-616)

Clinical studies were conducted in China in patients who had few (sometimes none) remaining options for therapy in acute myelogenous leukemia (AML). These patients were refractory to standard therapy and had debilitating symptoms. **Findings showed that some patients were put into partial remission and established the short term safety for the intravenous administration of PD-616.**

Encouraged by the clinical results from China, Roger Strair MD, PhD, a leading oncologist at The Cancer Institute of New Jersey (CINJ), at the University of Medicine and Dentistry of N.J. (UMDNJ), obtained an investigator IND, and conducted a **Phase 1 study** in patients the majority of whom also had relapsed/refractory AML. Based on Phase 1 findings, Biosuccess Biotech was encouraged by Dr. Strair to conduct a Phase 2 study in relapsed/refractory AML. Currently, a Phase 2 study is underway and the recruitment of refractory AML patients is actively done by Dr. Strair.

AIDS/HIV Studies with TPA (PD-616)

Three preliminary experiments, part of the clinical research process, were conducted in China on AIDS/HIV. These patients had few treatment options, as they presented many of the injurious effects of this disease and were refractory to standard anti-AIDS drugs. **Following treatment with PD-616, there was a disappearance of symptoms and a return to normal in almost all patients. In the third clinical study, the number of CD4 T-cells was somewhat reduced while the concentration of the virus in blood increased in all patients in 30 days after starting PD-616 treatment, but was almost undetectable at 60 days.** These results are clinical evidence that support the unique mechanism of action proposed for PD-616 in AIDS/HIV. Future clinical studies are needed, but it appears that PD-616 can be a totally new and highly effective drug for the treatment of AIDS. In order to confirm these clinical findings, Biosuccess Biotech Co. Ltd. has plans to conduct rigorously controlled clinical trials in the U.S. during a large Phase 2 study.

Legal Grounds

Biosuccess Biotech is protected by an issued "use patent" that provides sole rights to use the intravenous administration of PD-616 for therapeutic purposes (2001).

A patent application was filed on the use of PD-616 to treat AML in January, 2007. In January, 2008, a patent application was filed for the use of PD-616 in HIV/AIDS and includes coverage of many other phorbol ester structures in the PD-616 chemical class.

Biosuccess Biotech Co. Ltd. has 20 years exclusive rights to the use of PD-616 in AML and HIV/AIDS, beginning with January 30th, 2008.

In June 2011, AML Phase 2 protocol was approved by FDA.

Company History

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EXHIBIT C



US006063814A

United States Patent [19]
Chang et al.

[11] **Patent Number:** **6,063,814**
 [45] **Date of Patent:** **May 16, 2000**

[54] **PHORBOL ESTERS AS ANTI-NEOPLASTIC
 AND WHITE BLOOD CELL ELEVATING
 AGENTS**

[76] Inventors: **Richard L. Chang**, 107 Konner Ave.,
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 Henan, China

[21] Appl. No.: **08/837,085**

[22] Filed: **Apr. 14, 1997**

[51] **Int. Cl.⁷** **A61K 31/21**

[52] **U.S. Cl.** **514/510**

[58] **Field of Search** 514/510

[56] **References Cited**
PUBLICATIONS

Shih et al., Carcinogenesis (1993), 14(4), 709–12, 1993.

Primary Examiner—Jerome D. Goldberg
Attorney, Agent, or Firm—Bernard S. Leon

[57] **ABSTRACT**

Phorbol esters and particularly phorbol-12-myristate-13-acetate (TPA) are described as effective in treating patients with neoplastic diseases such as leukemia as well as in increasing the white blood cell count.

20 Claims, No Drawings

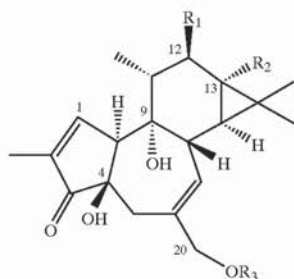
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PHORBOL ESTERS AS ANTI-NEOPLASTIC AND WHITE BLOOD CELL ELEVATING AGENTS

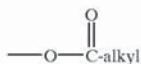
BRIEF DESCRIPTION OF THE INVENTION

The invention relates to treating neoplastic disease such as leukemia and increasing the white blood cell counts in patients suffering from neoplastic diseases or undergoing chemotherapy by a method which comprises administering parenterally to patients an effective amount of a phorbol ester of the Formula:

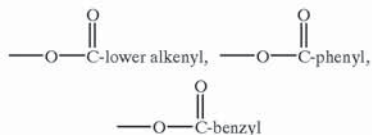


or isomers thereof

wherein R_1 and R_2 are selected from the group consisting of hydrogen,



wherein the alkyl group contains 1 to 15 carbon atoms,



and substituted derivatives thereof. At least one of R_1 and R_2 is other than hydrogen and R_3 is selected from the group consisting of hydrogen and



Preferred are Compounds of the Formula I wherein one of R_1 and R_2 is selected from the group consisting of



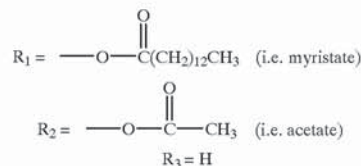
more preferably higher chain alkyl groups, especially decanoate or myristate and the other is

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and R_3 is hydrogen.

Especially preferred is a compound of the formula I where



i.e. phorbol-12-myristate-13-acetate or as it is also known 12-O-tetradecanoylphorbol-13-acetate (herein TPA)

The term "lower alkyl" or "lower alkenyl" as used herein shall mean moieties containing 1-7 carbon atoms. In the Compounds of the Formula I, the alkyl or alkenyl groups may be straight or branched chain and preferably contain at least one of R_1 or R_2 , a long chain carbon moiety (decanoate or myristate).

The alkyl, alkenyl, phenyl and benzyl groups may be unsubstituted or substituted with halogen, preferably, chlorine, fluorine or bromine, nitro, amino and similar type radicals.

BACKGROUND OF THE INVENTION

The compounds of the Formula I are generally known to be tumor promoters and as being highly irritant to skin and the mucous membrane.

The preferred exemplar TPA is a biologically active natural compound which can be extracted from croton oil. TPA has been known for many years to be a co-carcinogen or tumor promoter. See Merck Index, 11th Edition, Page 1164 No. 7306. It is also known to be a highly potent irritant to skin and to be harmful if ingested orally. In a product brochure distributed by Chemsyn Science Laboratories of Lenexa, Kansas, TPA is described as an extremely potent mouse skin cancer promoter and as a powerful mitogen in cell cultures. The product brochure warns the user to treat TPA with extreme care. The literature discloses that TPA induces differentiation in the stable human promyelocytic leukemic cell line HL-60. Weinberg, JP (Science 213:655-657, 1981) further discloses that TPA causes differentiation of cells of the human leukemia cell line HL-60 to nondividing macrophage-like cells. These differentiated cells are cytotoxic for tumor cells including current, untreated HL-60 cells in vitro. However, nowhere in the prior art has it been suggested that compounds of the Formula I when delivered parenterally to humans would be effective in treating neoplastic diseases or in raising the white blood cell count, much less without significant unwanted side effects.

Leukemia is a neoplastic disease in which white corpuscle maturation is arrested at a primitive stage of cell development. The disease is characterized by an increased number of leukemic blast cells in the bone marrow and by varying degrees of failure to produce normal hematopoietic cells. The condition may be either acute or chronic. Leukemias are further typically characterized as being lymphocytic or myelocytic. Acute lymphocytic leukemia (ALL) arises in lymphoid tissues and ordinarily first manifests its presence in bone marrow. Acute myelocytic leukemia (AML) arises

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from bone marrow hematopoietic stem cells or their progeny. The term "acute myelocytic leukemia" subsumes several subtypes of leukemia e.g. myeloblastic leukemia, promyelocytic leukemia and myelomonocytic leukemia.

Chronic myelogenous leukemia is characterized by abnormal proliferation of immature granulocytes, for example, neutrophils, eosinophils and basophils, in the blood, bone marrow, the spleen, liver and sometimes in other tissues. A large portion of chronic myelogenous leukemia patients develop a transformation into a pattern indistinguishable from the acute form of the disease. This change is known as the "blast crises". The present invention is generally suitable for treating leukemias, as well as other neoplastic diseases.

DETAILED DESCRIPTION OF THE INVENTION

Compounds of the Formula I are useful as anti-tumor agents in patients suffering from neoplastic diseases and for raising the white blood cell count in patients suffering from neoplastic diseases such as leukemia and other forms of tumors such as solid tumors and undergoing chemotherapy.

The preferred compound TPA has demonstrated in humans the ability to reduce the abnormal bone marrow profile in patients with AML and other types of leukemia to the point where the patient can be considered to be in remission. Of the patients treated with TPA, all had been diagnosed as having progressed to an acute form of leukemia and the prognosis for a favorable outcome was not very bright. Prior to the administration of TPA, all of the patients had received various forms of conventional chemotherapy including hydroxyurea, busulfan and Ara-C etc without success originally or because of the development of resistance to these drugs. Upon administration of TPA to these refractory patients, clinical remission was achieved in a relatively short time. In addition, during and after the treatment with TPA, there was no bone marrow suppression, infection or bleeding. Many of the patients have been in clinical remission for over six months from the time the treatment with TPA first started.

Additionally, the Compounds of the Formula I can be used to treat patients who are undergoing chemotherapy for the treatment of solid tumors as a method of elevating their white blood cell counts (leukocytes). Chemotherapeutic agents are known to exert toxic effects on certain normal cells in the body. The white blood cells in the body that are responsible for helping the body fight off infections are especially sensitive to chemotherapeutic agents. If these infection fighting cells, (the white blood cells) fall to very low levels in the patient receiving chemotherapy, the patient will become more susceptible to serious infection. TPA has shown the propensity to help speed the rapid recovery of the infection fighting cells, both after and during chemotherapy treatment and therefore TPA is especially useful in reducing the chances of a patient developing serious infections. Often the elevation of the white blood cell count occurs within one day of treatment. The present invention is useful in raising the white blood cell count in patients undergoing chemotherapy for all types of solid tumors such as breast, lung, prostate and colon cancers. TPA helps to maintain adequate levels of white blood cells or infection fighting cells. These cells work by surrounding and destroying bacteria that may have entered the body. TPA, by preventing the number of white blood cells from falling to low levels for long periods of time, lessens the potential for infection, the use of antibiotics and longer hospital stays. Generally by increasing the white blood cell count, the body is reprovided with an important component of its immune system.

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Because of the ability to elevate the white blood cell count, the present invention may also be useful in any patient with compromised white blood counts including patients suffering from AIDS.

Also, compounds of the Formula I in animal studies have evidenced the ability to inhibit solid tumor growth in laboratory animals.

Dosage delivery systems, preferably aqueous dosage delivery systems, suitable for parenteral administration of compounds of the Formula I in a pharmaceutical acceptable carrier, can be prepared by dissolving a Compound of the Formula I in an appropriate solvent which is miscible, dispersible or soluble with water, such as an alcohol e.g. ethanol, propanol, isopropanol and the like. Other water soluble solvents suitable for the purpose of the present invention include glycols such as propylene glycol or polyethylene glycol, glycerine (glycerol), glycerolfomal and the like. There can be added to the dosage forms antimicrobial preservatives such as benzyl alcohol, phenol, cresol (ortho, meta or para or mixtures of the foregoing) and phenylethylalcohol. There can also be added low concentrations of surfactants known to be suitable for intravenous use at low concentrations including Emulphor EL-620, Cremophor EL, Polysorbate 80 (Tween 80) or Polysorbate 20 (Tween 20).

Any solvent or mixtures of solvents and/or preservative and/or surfactant can be selected by the person skilled in the art as the pharmaceutically acceptable carrier in accordance with conventional practices for preparing parenteral dosage formulations. All that is required of a component of the pharmaceutically acceptable carrier to be suitable for the purposes of the present invention is that it be safe when injected into a human; is miscible, dispersible or soluble in water; has no cytotoxicity; and does not diminish the shelf life of the pharmaceutical formulation so that it may be stored.

The compounds of the Formula I in the treatment of neoplastic diseases such as leukemia or for raising white blood cell counts can be administered parenterally (I.V.) in dosage amounts from about 0.001 mg per dose to about 1.5 mg per dose, for about 1-7 times per week for about 1-10 weeks; more preferable from about 0.05 to about 1 mg, 1-7 times per week, for 1-7 weeks; and still more preferably from about 0.1 mg to about 0.6 mg, 1-7 times per week for about 1-7 weeks. The most preferred dosage form is delivered through I.V. infusion and contains 0.1 mg, 0.25 mg or 0.5 mg per dose. The course of therapy preferred is 1-7 weeks with 1 mg being administered over a week in divided doses.

In patients receiving chemotherapy for solid tumors, the most preferred time for administering a single dose of a compound of the Formula I is about the time the patient is to receive or has just undergone a course of chemotherapy designed to combat the solid tumors.

The precise dosage amount and the duration of administration of a compound of the Formula I will depend on the exigencies of the medical situation and the judgement of the physician treating the patient in accordance with conventional practice among medical professionals. The exact dose will depend upon such factors as the age, weight and condition of the patient, the frequency of administration and the manner in which the patient responds to the treatment.

EXAMPLE I

The following compounds are illustrative of the compounds encompassed by Formula I which are suitable for the purposes of the present invention. These compounds are commercially available.

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- 1) Phorbol 13-Butyrate
- 2) Phorbol 12-Decanoate
- 3) Phorbol 13-Decanoate
- 4) Phorbol 12,13-Diacetate
- 5) Phorbol 13,20-Diacetate
- 6) Phorbol 12,13-Dibenzoate
- 7) Phorbol 12,13-Dibutyrate
- 8) Phorbol 12,13-Didecanoate
- 9) Phorbol 12,13-Dihexanoate
- 10) Phorbol 12,13-Dipropionate
- 11) Phorbol 12-Myristate
- 12) Phorbol 13-Myristate
- 13) Phorbol 12-Myristate-13-Acetate (also known as TPA or PMA)
- 14) Phorbol 12,13,20-Triacetate
- 15) 12-Deoxyphorbol 13-Angelate
- 16) 12-Deoxyphorbol 13-Angelate 20-Acetate
- 17) 12-Deoxyphorbol 13-Isobutyrate
- 18) 12-Deoxyphorbol 13-Isobutyrate-20-Acetate
- 19) 12-Deoxyphorbol 13-Phenylacetate
- 20) 12-Deoxyphorbol 13-Phenylacetate 20-Acetate
- 21) 12-Deoxyphorbol 13-Tetradecanoate
- 22) Phorbol 12-Tiglate 13-Decanoate
- 23) 12-Deoxyphorbol 13-Acetate
- 24) Phorbol 12-Acetate
- 25) Phorbol 13-Acetate

EXAMPLE 2

Formulation Type A

0.10, 0.125, 0.25 or 0.5 mg of TPA was dissolved in 1.3 ml 95–100% U.S.P. ethanol and 0.7 ml saline. Under sterile conditions, TPA was first dissolved in ethanol, then saline was added, mixed vigorously, bacteriologically filtered, and stored in sealed sterile amber vials containing either 0.10 mg/2 ml, 0.125 ml/2 ml or 0.25 mg/2 ml, 0.5 mg/2 ml.

Formulation Type B

0.10, 0.125, 0.25 or 0.5 mg of TPA was dissolved in 0.2 ml of ethanol, 1.2 ml of isopropanol and 0.6 ml saline. Under sterile conditions, TPA was first dissolved in the ethanol and isopropanol, then saline was added, and the mixture was vigorously mixed, bacteriologically filtered and stored in sealed sterile amber vials containing either 0.10 mg/2 ml, 0.125 ml/2 ml or 0.25 mg/2 ml or 0.5 mg/2 ml.

Analytical results showed that there is no chemical change in the TPA solutions stored in the dark at cold temperature for up to one year; also, there is no chemical change in the TPA solutions stored in the dark at room temperature up to two months.

EXAMPLE 3

1. Effect of TPA in a Human Promyelocytic Leukemia Cell Line (HL-60):

HL-60 cells at 2×10^6 cells/ml were treated with TPA. The final concentrations of TPA were 10, 20, or 100 ng/ml. The ethanol content was less than 0.01%. After 3 hours of TPA treatment, the cells stopped proliferating and cell aggregation and attachment to the dish were observed. After 48 h of treatment, there were morphological changes. After 4–6 days, morphological and cellular biochemical studies showed that the majority of the cells were induced to differentiate to macrophages in a dose-dependent manner.

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EXAMPLE 4

(2) TPA+Low Doses of Ara-C:

The treatment of HL-60 cells with low doses of TPA (20 ng/ml) or Ara-C (100 ng/ml) demonstrated that Ara-C could induce cell differentiation, and TPA at low concentration is a weak cell differentiation-inducing agent. The combination treatment of HL-60 cells with TPA and Ara-C induced the HL-60 cells to differentiate synergistically.

EXAMPLE 5

10 Effect of TPA in Mice Injected With S180 (Sarcoma 180) Tumor Cells:

Eight groups of Kwen-Ming mice containing 7 mice per group were used in the following experiment. Two groups were untreated and six groups received the drug.

Each Kwen-Ming mouse was injected with 5×10^6 S180 cells at the under-arm position. After 24 or 72 h, the animals were given TPA i.p. or locally at the tumor site. The injected doses of TPA were 50, 100 and 200 $\mu\text{g/kg/d}$ for 7 days. The animals were sacrificed 24 hrs after the final TPA treatment and the tumors were weighed to calculate the extent of the tumor growth inhibition. The study showed that the tumor growth was inhibited by 41.7%, 54.8% and 30.4%, respectively, in mice that were injected i.p. with 50, 100 or 200 $\mu\text{g/kg}$ TPA daily for 7 days. The tumor growth was inhibited by 35.5%, 49.3% and 59.2%, respectively, in mice that were injected daily for 7 days with 50, 100 or 200 $\mu\text{g/kg}$ TPA locally at the tumor site in comparison to the control mice. Pathological studies showed that the tumor cells were differentiated after the TPA treatment.

EXAMPLE 6

Effect of TPA in Mice Injected with B16 Tumor Cells:

Four groups of C57 mice were used in the experiment. Each group contained 7 mice and one group was untreated. Each C57 mouse was injected with 0.2 ml of supernatant of a 1:6 w/v homogenate of B16 cells at the under-arm position. On the third day, each treatment group was given TPA i.p. at 50, 100 or 200 $\mu\text{g/kg/d}$ for 8 days. The animals were sacrificed after the treatment, the tumors were weighed, and the rates of inhibition of tumor growth were 40.0%, 59.4% and 32.1%, respectively, which were all statistically different from the control group.

EXAMPLE 7

45 Effect of TPA on the Peripheral White Blood Cells (WBC) and Hemoglobin (Hb) Counts in S180 Cell-Injected Mice:

S180 cells were injected into mice. On the third day, the mice were given TPA i.p. at 50, 100 or 200 $\mu\text{g/kg/d}$ for 7 days. On the second day after the treatment was completed, blood samples were taken from the tails of the treated mice for WBC and Hb analyses. The WBC counts for the treated groups (50, 100, or 200 $\mu\text{g/kg/d}$ for 7 d) were 16.1 ± 7.4 , 18.7 ± 3.0 and $20.7 \pm 3.4 \times 10^9/\text{L}$, respectively; the WBC count for the control group was $13.6 \pm 1.8 \times 10^9/\text{L}$. The Hb of the treated groups were 136 ± 11 , 149 ± 12 and 149 ± 10 g/L, and the Hb of the control group was 134 ± 15 g/L. The results indicate that i.p. injection of TPA could increase the peripheral WBC counts in mice in a dose-dependent manner, whereas the Hb levels were not greatly affected in TPA treated mice when compared to the control mice.

EXAMPLE 8

Study on the Clinical Use of TPA in Humans

1. Dose Ranging Study.

Due to the strong local irritation caused by TPA application, TPA was given to patients by i.v. infusion. TPA solution in a sterile syringe was injected into 200 ml of saline and mixed well for i.v. infusion.

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2. The Toxicity and Side Effects of Different TPA Doses Administered Clinically:

(1) TPA given at 1 mg/patient/week:

One mg TPA in solution was mixed well with 200 ml of saline for i.v. infusion which was completed in 1 h at the rate of 16 $\mu\text{g}/\text{min}$. One hour after TPA administration, patients started to have chills which lasted for about 30 min, followed by fever, (the patients' temperature reached 37.5–39.5° C. which lasted for 3–5 h, then returned to normal) with light to heavy perspiration. The above symptoms could be alleviated by giving the patients glucocorticoids. TPA at this dose caused a minority of patients to bleed, several patients suffered for a short period of time difficulty in breathing, and Hb was detected in the urine. However, these side effects were short lived and reversible. The cardiac, hepatic, renal and pulmonary functions were all found to be normal.

(2) TPA given at 0.5 mg/patient \times 2/week: (two doses a week)

0.5 mg of TPA in solution was mixed well with 200 ml of saline for i.v. infusion which was completed in 1 h at the rate of 8 $\mu\text{g}/\text{min}$. The reactions after administration were similar to that of the 1 mg TPA dosage, but to a lesser extent than the 1 mg dose. The patients tolerated the lower dose more easily. Occasionally, Hb was detected in patients urine. Difficulty in breathing was not observed. The cardiac, hepatic, renal and pulmonary functions were all normal.

(3) TPA given at 0.25 mg/patient \times 4/week:

0.25 mg of TPA in solution was mixed well with 200 ml of saline for i.v. infusion which was completed in 1 h at the rate of 4 $\mu\text{g}/\text{min}$. After the administration, symptoms such as chills and fever were also observed, but to a much lesser extent than with the higher dosages. No Hb was detected in the urine, and no patient suffered difficulty in breathing. The cardiac, hepatic, renal and pulmonary functions were all normal.

After comparing the above three dosages, 0.25 mg/person \times 4/week and 0.5 mg/person \times 2/week are considered to be preferred dosages of TPA.

EXAMPLE 9

The results obtained upon treatment of patients with TPA as presented in tabular form and in subsequent examples.

TABLE 1

Clinical Summary of Clinical Efficacy of TPA in the Five Cases Representing Chronic Myelocytic Leukemia Having Progressed to Acute Myelocytic Leukemia Before TPA Administration (Subjects 1–5) and Five Cases of Other Leukemias (Subjects 6–10)		
Subject No.	Bone marrow Myeloblast and promyelocyte percent of total cells	
	Before TPA	After TPA
1	30	2.5
2	36	3.0
3	90	2.0
4	67.5	4.5
5	27.5	1.5
6	48	3
7	16	10
8	80.8	17
9	(Aplastic anemia)	(TPA terminated)
10	(9% early in TPA treatment)	0

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TABLE 2

Clinical Summary of TPA induced White Blood Cell Changes (WBC) in Patients with Solid Tumors Undergoing Chemotherapy		
Subject No.	WBC ($\times 10^9/\text{liter}$)	
	Before TPA	Peak after TPA
11	0.7	6.8
12	3.0	4.5
13	0.9	2.5
14	3.8	8.0
15	2.4	7.1
16	2.4	5.2
17	2.0	4.4
18	2.4	4.0
19	2.9	5.1
20	0.7	2.7
21	1.1	1.5
22	1.9	7.6
23	2.3	3.9
24	1.1	5.3
25	2.1	6.4
26	3.6	5.6

EXAMPLE 10

In the subjects identified as (1) through (5) below, chronic myelocytic leukemia had progressed to acute myelocytic leukemia before treatment with TPA.

Subject No. (1) T.S., male, 32, patient No. 28879. Blood profile before TPA treatment: Hb: 28 g/L; WBC: $1.0 \times 10^9/\text{L}$, platelet: $135 \times 10^9/\text{L}$. Bone marrow profile before TPA treatment: myeloblast+promyelocyte: 30%. TPA treatment: 1 mg/week (0.25 mg administered four times) for two weeks. Blood profile after treatment: Hb: 86 g/L; WBC: $2.8 \times 10^9/\text{L}$, platelet: $283 \times 10^9/\text{L}$. Bone marrow profile after TPA treatment: myeloblast+promyelocyte: 2.5%.

Subject No. (2) C.J., male, 30, patient No. 29926. Diagnosis: chronic myelocytic leukemia became acute myelocytic leukemia before treatment. Blood profile before TPA treatment: Hb: 94 g/L; WBC: $9.8 \times 10^9/\text{L}$, platelet: $63 \times 10^9/\text{L}$. Spleen: 3 cm below the rib cage. Bone marrow profile before TPA treatment: myeloblast+promyelocyte: 36%. TPA treatment: 1 mg/week for 5 weeks. Blood profile after treatment: Hb: 104 g/L; WBC: $4.9 \times 10^9/\text{L}$, platelet: $80 \times 10^9/\text{L}$. Spleen: 0.5 cm below the rib cage. Bone marrow profile after TPA treatment: myeloblast+promyelocyte: 3%.

Subject No. (3) Z.K., male, 42, patient No. 18102. Diagnosis: chronic myelocytic leukemia became acute myelocytic leukemia before treatment. Blood profile before TPA treatment: Hb: 70 g/L; WBC: $27.5 \times 10^9/\text{L}$, platelet: $21 \times 10^9/\text{L}$. Bone marrow profile before TPA treatment: myeloblast+promyelocyte: 90%. TPA treatment: 1 mg/week for 7 weeks. Blood profile after treatment: Hb: 96 g/L; WBC: $22 \times 10^9/\text{L}$, platelet: $70 \times 10^9/\text{L}$. Bone marrow profile after TPA treatment: myeloblast+promyelocyte: 2%.

Subject No. (4) W.F. male, 25, patient No. 21315. Diagnosis: chronic myelocytic leukemia became acute myelocytic leukemia before treatment. Blood profile before TPA treatment: Hb: 87 g/L; WBC: $19 \times 10^9/\text{L}$, platelet: $150 \times 10^9/\text{L}$. Bone marrow profile before TPA treatment: myeloblast+promyelocyte: 67.5%. TPA treatment: 1 mg/week for 7 weeks. Blood profile after treatment: Hb: 45 g/L; WBC: $53.5 \times 10^9/\text{L}$, platelet: $210 \times 10^9/\text{L}$. Bone marrow profile after TPA treatment: myeloblast+promyelocyte: 4.5%.

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Subject No. (5) D.H., male, 38, patient No. 23965. Diagnosis: chronic myelocytic leukemia progressed to acute myelocytic leukemia. Blood profile before TPA treatment: Hb: 84 g/L; WBC: 36.6×10^9 /L, platelet: 290×10^9 /L. Bone marrow profile before TPA treatment: myeloblast+promyelocyte: 27.5%. TPA treatment: 1 mg/week for 2 weeks. Blood profile after treatment: Hb: 84 g/L; WBC: 27.3×10^9 /L, platelet: 170×10^9 /L. Bone marrow profile after TPA treatment: myeloblast+promyelocyte: 1.5%.

All the above patients had received various regimens of chemotherapy prior to the TPA treatment, including hydroxyurea, busulfan, and Ara-C, etc. but none was effective at the start of TPA treatment. Before the administration of TPA, patients received injection of 6×10^5 units of vitamin D₃ (VD₃)/person for 2 days; after the TPA administration, patients received i.v. infusion of 40 mg of Ara-C/dx3. After the treatment, the patients all achieved clinical remission in bone marrow parameters in a short time. In addition, during and after the treatment, there was no bone marrow suppression, nor infection or bleeding. These patients have been in clinical remission for over 6 months.

EXAMPLE 11

Other Types of Leukemia:

Subject No. (6) Y.P., male, 57. Diagnosed as AML-M3. Symptoms began in January, 1995. Blood profile: Hb: 60 g/L, WBC: 0.4×10^9 /L, platelet: 40×10^9 /L. Bone marrow profile: myeloblast+promyelocyte: 48%. The TPA treatment period was 1 mg/week for three weeks, and 6×10^5 units VD₃/dx3 were injected prior to the treatment. After the first treatment period, blood profile: Hb: 118 g/L, WBC: 4.1×10^9 /L, platelet: 80×10^9 /L. Bone marrow profile: myeloblast+promyelocyte: 3%, which met the standard for AML-M3 remission. The patient has been in remission after treatment for at least 6 months.

Subject No. (7) M.W., male, 67. Diagnosis: MDS-REAB accompanied by an increased number of monocytes. Four months of oral VP16 administration failed to produce results. The patient started to receive a combination treatment of 1,25-(OH)₂ VD₃ +TPA+low dose Ara-C. TPA dosage: 0.25–0.5 mg (1 mg per week) for eleven weeks. Blood profile before TPA treatment: Hb: 36 g/L; WBC: 4.0×10^9 /L, platelet: 29×10^9 /L. Myeloblast: 2%, Promyelocyte: 4%, Myelocyte: 3%, Neutrophil: 60%, Lymphocyte: 25%, Monocyte 6%. Bone marrow profile before treatment: active in proliferation, myeloblast: 8%, promyelocyte: 8%. Spleen: 3 cm below the rib cage. After the treatment: Spleen: 0.5 cm below the rib cage. Blood profile: Hb: 42 g/L; WBC: 10.2×10^9 /L, platelet: 34×10^9 /L. Neutrophil: 80%, Lymphocyte: 19%, Monocyte 1%. Promyelocytes were not detected. Bone marrow profile: active in proliferation, myeloblast: 4%, promyelocyte: 6%.

Subject No. (8) L.Q., male, 36. Diagnosis: AML-M3. Treatment with retinoic acid (RA) at 80 mg/dayx50 was not successful. Blood profile before the treatment with TPA: Hb: 45 g/L, WBC: 1.0×10^9 /L, platelet: 35×10^9 /L. Bone marrow profile: very active in proliferation, myeloblast+promyelocyte: 80.8%. Blood profile after the TPA treatment: Hb: 66 g/L, WBC: 2.2×10^9 /L, platelet: 223×10^9 /L. Bone marrow profile: active in proliferation, myeloblast+promyelocyte: 17%.

Subject No. (9) Z.H., female, 21. Diagnosis: bone marrow suppression after receiving chemotherapy for chronic myelocytic leukemia, secondary aplastic anemia. The patient was treated with busulfanum (Busulfan) for 3 months. Blood profile before TPA treatment: Hb: 43 g/L, WBC: 1.6×10^9 /L, platelet: 26×10^9 /L. Bone marrow pro-

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file: aplastic anemia. TPA dosage: 0.25 mgx2. Blood profile after the TPA treatment: Hb: 32 g/L, WBC: 1.9×10^9 /L, platelet: 57×10^9 /L. Due to severe anemia, the TPA treatment was terminated.

Subject No. (10) L.N., female, 26. Diagnosis: CML. The patient had been treated with chemotherapy using the combination of homoharringtonine and Ara-C. Blood profile before TPA treatment: Hb: 98 g/L; WBC: 2.0×10^9 /L, platelet: $10^2 \times 10^9$ /L. 0.25 mg TPA administered to the patient once. Blood profile after treatment: Hb: 96 g/L; WBC: 2.0×10^9 /L, platelet: 112×10^9 /L. On the second day after TPA treatment: myeloblast+promyelocyte: 4%, myelocyte 5%. On the fifth day after the TPA treatment, these types of blood cells completely disappeared.

EXAMPLE 12

Patients undergoing chemotherapy for the treatment of solid tumors.

Subject No. (11) L.X., female, 50. Diagnosis: malignant lymphoma. The patient had received adramycin, vincristine, and hormonal treatment. The blood cell counts were decreased to: Hb: 78 g/L, WBC: 0.7×10^9 /L, platelet: 245×10^9 /L. 0.25 mg TPA was administered to the patient 4 times. The blood cell counts improved to: Hb: 76 g/L, WBC: 6.8×10^9 /L, platelet: 331×10^9 /L. Chemotherapy was then continued for 5 more days, and followed by one dose of 0.5 mg TPA. The WBC count was maintained at 3.0×10^9 /L. The patient is still receiving treatment.

Subject No. (12) Y.G., female, 45. Diagnosis: brain tumor. Blood profile after chemotherapy was: Hb: 119 g/L, WBC: 3.0×10^9 /L, platelet: 399×10^9 /L. 0.25 mg TPA was given to the patient once. On the day after the TPA treatment, the blood profile was Hb: 123 g/L, WBC: 4.5×10^9 /L, platelet: 436×10^9 /L. The patient received further chemotherapy.

Subject No. (13) G.F., male, 60. Diagnosis: lung cancer. After chemotherapy, his blood cell counts were decreased to: Hb: 76 g/L, WBC: 0.9×10^9 /L, platelet: 100×10^9 /L. 0.25 mg TPA was given to the patient twice. On the day after the TPA treatment, Hb: 74 g/L, WBC: 2.5×10^9 /L, platelet: 110×10^9 /L. The patient is still receiving treatment.

Subject No. (14) Z.R., female, 44. Diagnosis: breast cancer. The WBC after chemotherapy was 3.8×10^9 /L. 0.25 mg of TPA was given to the patient once. The WBC on the day after the TPA treatment was 8.0×10^9 /L.

Subject No. (15) C.Z., female, 75. Diagnosis: Esophageal Cancer. Surgery was performed, followed by chemotherapy using cisplatin, 5-fluorouracil. Blood profile (before TPA): WBC: 2.4×10^9 /L; neutrophil: 83%, lymphocyte: 17%; platelet: 150×10^9 /L; RBC: 3.43×10^{12} /L; Hb: 107 g/L. TPA dosage: 0.25 mg. Blood profile (one day after TPA): WBC: 7.1×10^9 /L; neutrophil: 94%; lymphocyte: 6%; platelet: 77×10^9 /L; RBC: 3.33×10^{12} /L; Hb: 109 g/L. Blood profile (4 days after TPA): WBC: 4.4×10^9 /L; neutrophil: 97%; lymphocyte: 3%; platelet: 105×10^9 /L; RBC: 3.36×10^{12} /L; Hb: 112 g/L. Symptoms after TPA: Chill, fever, local irritation and slight headache. The cardiac, hepatic, renal and pulmonary functions were normal.

Subject No. (16) X.H., female, 60. Diagnosis: Esophageal Cancer. Surgery was performed, followed by chemotherapy using VP16, MTX, MMC and cisplatin. TPA dose: 0.25 mg. Blood profile (before TPA): WBC: 2.4×10^9 /L; neutrophil: 67%; lymphocyte: 23%; platelet: 101×10^9 /L; RBC: 3.45×10^{12} /L; Hb: 114 g/L. Blood profile

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(one day after TPA): WBC: $5.2 \times 10^9/L$; neutrophil: 87%; lymphocyte: 13%; platelet $60 \times 10^9/L$; RBC: $3.76 \times 10^{12}/L$; Hb: 122 g/L. Blood profile (2 days after TPA administration). WBC: $4.5 \times 10^9/L$; neutrophil 80%; lymphocyte: 20%; platelet: $64 \times 10^9/L$; RBC: $2.99 \times 10^{12}/L$; Hb: 109 g/L. Symptoms after TPA: chills, fever, local irritation, cardiac, hepatic, renal and pulmonary were normal.

Subject No. (17) Y.Z., female, 37. Diagnosis: breast cancer. Surgery was performed, followed by chemotherapy using CTX, MTX, and 5-FU. TPA dose: 0.25 mg \times 2 (Second dose was 4 days after 1st dose). Blood profile (before TPA): WBC: $2.0 \times 10^9/L$; neutrophil: 85%; lymphocyte: 15%; platelet: $106 \times 10^9/L$; RBC: $3.24 \times 10^{12}/L$; Hb: 107 g/L. Blood profile (3 days after first TPA dose): WBC: $2.9 \times 10^9/L$; neutrophil 83%; lymphocyte: 17%; platelet: $122 \times 10^9/L$; RBC: $3.36 \times 10^{12}/L$; Hb: 107 g/L. Blood profile (2 days after second TPA dose): WBC: $3.8 \times 10^9/L$; neutrophil: 84%; lymphocyte: 16%; platelet: $84 \times 10^9/L$; RBC: $3.47 \times 10^{12}/L$. Blood profile (4 days after second TPA dose): WBC: $4.4 \times 10^9/L$; neutrophil: 86%; lymphocyte: 14%; platelet $193 \times 10^9/L$; RBC: $3.49 \times 10^{12}/L$; Hb: 112 g/L. Symptoms after TPA: patient started to have chills which lasted for 2 hrs followed by fever, temperature reached 38° C. which lasted 4 hrs and local irritation. The cardiac, hepatic, renal and pulmonary functions were normal.

Subject No. (18) H.P., male, 56. Diagnosis: Colon cancer. Surgery was performed, followed by chemotherapy using Cisplatin, VP16, and 5-FU. TPA dose: 0.25 mg \times 2 (2nd TPA dose was administered 24 hrs after 1st TPA dose). Blood profile (before TPA): WBC: $2.4 \times 10^9/L$; neutrophil: 63%; lymphocyte: 37%; platelet: $208 \times 10^9/L$; RBC: $4.0 \times 10^{12}/L$; Hb: 104 g/L. Blood profile (one day after 2nd TPA dose): WBC: $4.0 \times 10^9/L$; neutrophil: 60%; lymphocyte: 40%; platelet: $198 \times 10^9/L$; RBC: $4.1 \times 10^{12}/L$; Hb: 112 g/L. Symptoms after TPA: chills, fever, local irritation. Cardiac hepatic, renal and pulmonary functions were normal.

Subject No. (19) Z.T., male, 66. Diagnosis: lung cancer metastasized to adrenal gland. Surgery was performed, followed by chemotherapy using MMC, VCR, and CTX. TPA dosage: 0.25 mg \times 2 (2nd TPA dose was administered 24 hrs after 1st TPA dose). Blood profile (before TPA): WBC: $2.9 \times 10^9/L$; neutrophil: 76%; lymphocyte: 24%; platelet: $227 \times 10^9/L$; RBC: $3.33 \times 10^{12}/L$; Hb: 100 g/L. Blood profile (one day after second TPA dose): WBC: $5.1 \times 10^9/L$; neutrophil: 82%; lymphocyte: 18%; platelet: N/A; RBC: N/A; Hb: 93 g/L. Blood profile (2 days after 2nd TPA dose): WBC: $5.0 \times 10^9/L$; neutrophil: 80%; lymphocyte: 20%; platelet: N/A; RBC: $3.25 \times 10^{12}/L$; Hb: 101 g/L. Symptoms after TPA: chills, fever, local irritation. Cardiac, hepatic renal and pulmonary functions were normal.

Subject No. (20) J.Z., male, 68. Diagnosis: esophageal cancer metastasized to liver, lung and brain. The patient received chemotherapy using Taxol, cisplatin, 5-FU and Semustial. Total TPA dosage: 2mg. Blood profile (before TPA): WBC: $0.7 \times 10^9/L$; neutrophil: 29%; lymphocyte: 71%; platelet: N/A; RBC: $2.82 \times 10^{12}/L$; Hb: 87 g/L. TPA treatment schedule. On the first and third day, 0.25 mg was given and on the 5th, 7th and 9th day 0.5 mg of TPA was given. Blood profile (at day 2): WBC: $0.9 \times 10^9/L$; neutrophil: 66%; lymphocyte: 34%; platelet: $82 \times 10^9/L$; RBC: $2.17 \times 10^{12}/L$; Hb: 72 g/L. Blood profile (at day 4): WBC: $1.1 \times 10^9/L$; neutrophil: 91%; lymphocyte: 9%; platelet: $39 \times 10^9/L$; RBC: $2.09 \times 10^{12}/L$; Hb: 58 g/L. Blood profile (at day 6): WBC: $1.9 \times 10^9/L$; neutrophil: 95%;

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lymphocyte: 5%; platelet: $43 \times 10^9/L$; RBC: $1.9 \times 10^{12}/L$; Hb: 70 g/L. Blood profile (at day 8): WBC: $2.3 \times 10^9/L$; neutrophil: 91%; lymphocyte: 9%; platelet: $90 \times 10^9/L$; RBC: $1.71 \times 10^{12}/L$; Hb: 61 g/L. Blood profile (at 11th day): WBC: $2.7 \times 10^9/L$; neutrophil: 85%; lymphocyte: 15%; platelet: $37.6 \times 10^9/L$; RBC: $2.91 \times 10^{12}/L$; Hb: 61 g/L. Blood profile (at day 13): WBC: $1.9 \times 10^9/L$; neutrophil: 90%; lymphocyte: 10%; platelet: $32 \times 10^9/L$; RBC: $1.73 \times 10^{12}/L$; Hb: 57 g/L. Symptoms after TPA: Chills at 5th day which lasted about one hour. Cardiac, hepatic, renal and pulmonary functions were normal.

Subject No. (21) D.Y., female, 32. Diagnosis: lymphoma metastasized to bone marrow. The patient was treated with chemotherapy using CTX, ADM, and VCR prior to TPA treatment. TPA dosage: 0.25 mg. TPA treatment schedule: 0.25 mg of TPA was administered on days 1 and 2. 0.5 mg of TPA was administered on days 3, 5, 6 and 8. Blood profile (before TPA): WBC: $1.1 \times 10^9/L$; neutrophil: 73%; lymphocyte: 27%; platelet: $144 \times 10^9/L$; RBC: $4.15 \times 10^{12}/L$; Hb: 142 g/L. Blood profile (at day 2): WBC: $0.6 \times 10^9/L$; neutrophil: N/A; lymphocyte: N/A; platelet: $69 \times 10^9/L$; RBC: $4.15 \times 10^{12}/L$; Hb: 117 g/L. Blood profile (at day 4): WBC: $0.6 \times 10^9/L$; neutrophil: 28%; lymphocyte: 72%; platelet: $68 \times 10^9/L$; RBC: $3.95 \times 10^{12}/L$; Hb: 109 g/L. Blood profile (at day 7): WBC: $0.8 \times 10^9/L$; neutrophil: 88%; lymphocyte: 12%; platelet: $60 \times 10^9/L$; RBC: $4.22 \times 10^{12}/L$; Hb: 110 g/L. Blood profile (at day 9): WBC: $1.5 \times 10^9/L$; neutrophil: 80%; lymphocyte: 2%; platelet: $69 \times 10^9/L$; RBC: $4.02 \times 10^{12}/L$; Hb: 112 g/L. Symptoms after TPA: No chills and fever, only local irritation. Cardiac, hepatic, renal and pulmonary functions same as before TPA treatment. Since this patient's lymphoma cells had metastasized to the bone marrow, she required a high dose of TPA (2.5 mg) and a longer treatment time (9 days) in order to induce a very low level of WBC.

Subject No. (22) X.Y., female, 34. Diagnosis: Nasopharyngeal carcinoma metastasized to neck lymph node. The patient was treated with chemotherapy using 5-FU, ADM, and MMX prior to treatment with TPA. Blood profile after chemotherapy (but before TPA treatment): WBC: $1.9 \times 10^9/L$; neutrophil: 89%; lymphocyte: 11%; Hb: 118 g/L. Blood profile (one day after administration of 0.25 mg): WBC $1.8 \times 10^9/L$; neutrophil: 79%; lymphocyte: 21%; Hb: 116 g/L. Blood profile (three days after TPA administration): WBC: $2.9 \times 10^9/L$; neutrophil: 73%; lymphocyte: 27%; Hb: 123 g/L. Blood profile (7 days after TPA administration): WBC: $7.6 \times 10^9/L$; neutrophil: 82%; lymphocyte: 18%; Hb: 118 g/L. Symptoms after TPA: Chills, fever (39.2° C.) continued for 4 hrs. Liver, kidney, heart and lung were functioning normally.

Subject No. (23) J.H., male, 55. Diagnosis: stomach (cardia) cancer, reoccurred after prior surgery. The patient had received 5-FU and MMC. before treatment with TPA. Blood profile (before TPA administration): WBC: $2.3 \times 10^9/L$; neutrophil: 52%; lymphocyte: 48%; Hb: 144 g/L. Blood profile (one day after 0.25 mg TPA administration): WBC: $1.9 \times 10^9/L$; neutrophil: 53%; lymphocyte: 47%; Hb: 123 g/L. Blood profile (four days after TPA): WBC: $3.9 \times 10^9/L$; neutrophil: 44%; lymphocyte: 56%; Hb: 129 g/L. Blood profile (seven days after TPA): WBC: $3.7 \times 10^9/L$; neutrophil: 48%; lymphocyte: 52%; Hb: 138 g/L. Symptoms after TPA: No chills. Low fever (37.8° C.). Functions of liver, kidney, heart and lung were normal.

Subject No. (24) W.L., male, 62. Diagnosis: multiple myeloma. The patient had received VCR, ADM, and DXM before treatment with TPA. Blood profile (before

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TPA administration): WBC: $1.1 \times 10^9/L$; neutrophil: 73%; lymphocyte: 27%; Hb: 112 g/L. Blood profile (one day after administration of 0.25 mg TPA): WBC: $5.3 \times 10^9/L$; neutrophil: 60%; lymphocyte: 40%; Hb: 139 g/L. Symptoms after TPA: No chills, no fever, no local irritation. Liver, kidney, heart and lung were functioning normally.

Subject No. (25) T.L., female, 42. Diagnosis: breast cancer.

The patient received chemotherapy treatment using CTX, MMC, and 5-FU. Blood profile (before TPA): WBC: $2.1 \times 10^9/L$; neutrophil: 72%; lymphocyte: 28%; Hb: 126 g/L. Blood profile (one day after administration of 0.25 mg of TPA): WBC: $6.4 \times 10^9/L$; neutrophil: 90%; lymphocyte: 10%; Hb: 126 g/L. Symptoms after TPA administration: No chills, no fever. Injection site was red, swollen in appearance and painful probably caused by the infusion needle. The symptoms disappeared the second day after they appeared. Liver, kidney, heart and lung were functioning normally.

Subject No. (26) Q.W., male, 56. Diagnosis: esophageal cancer which had metastasized to the liver after surgery.

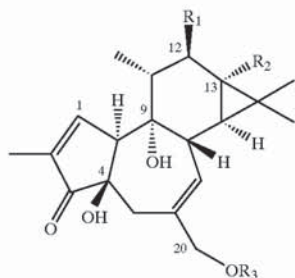
The patient had received chemotherapy using cisplatin and taxol. TPA dosage: 0.25 mg. Blood profile (before TPA administration): WBC: $3.6 \times 10^9/L$; neutrophil: 80%; lymphocyte: 20%; Hb: 124 g/L. Blood profile (one day after TPA administration): WBC: $4.2 \times 10^9/L$; neutrophil: 83%; lymphocyte: 17%; Hb: 120 g/L. Blood profile (2 days after TPA): WBC: $5.6 \times 10^9/L$; neutrophil: 81%; lymphocyte: 19%; Hb: 116 g/L. Symptoms after TPA administration: temperature reached $39^\circ C$. which lasted 3 hr. Stomach ache and diarrhea (which disappeared soon after). The cardiac, hepatic, renal and pulmonary functions were normal.

Abbreviations

VP16, Etoposide; MMC, Mitomycin C; MTX, Methotrexate; 5FU, 5-fluorouracil; CTX, Cyclophosphamide; CP, Cisplatin; VD₃, vitamin D₃; MDS-RAEB, Myelodysplastic syndrome-refractory anemia with excessor blasst; Ara-C, cytarabine; AML, Acute myelocytic leukemia; M1, AML without differentiation; M2, AML with maturation; M3, Acute promyelocytic leukemia; M4, Acute myelomonocytic leukemia; M5, Acute monocytic leukemia; RT, Retention time; WBC, White blood cells; Hb, Hemoglobin.

What is claimed is:

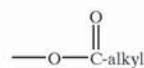
1. A method of treating leukemia which comprises administering parenterally to patients afflicted with leukemia, an effective amount of a compound of the Formula



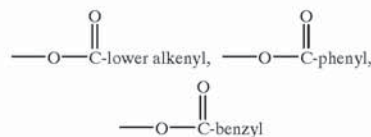
or isomers thereof

wherein R₁ and R₂ are selected from the group consisting of hydrogen,

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wherein the alkyl group contains 1–15 carbon atoms,



or substituted derivatives thereof, at least one of R₁ and R₂ is other than hydrogen and R₃ as selected from the group consisting of hydrogen and



2. A method as in claim 1 wherein the effective amount is from about 0.001 mg to about 1.5 mg per single dose administered 1–7 times per week for 1–7 weeks.

3. A method as in claim 2 wherein the effective amount is from about 0.05 mg to about 1 mg. per dose delivered 1–7 times per week for 1–7 weeks.

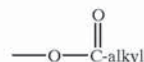
4. A method as in claim 3 wherein the effective amount is from about 0.05 mg to about 0.6 mg. per dose.

5. A method as in claim 4 wherein the effective amount is 1 mg. per week for 1–7 weeks.

6. A method as in claim 5 wherein the leukemia is myelocytic.

7. A method as in claim 6 wherein at least one of R₁ or R₂ is decanoate or myristate.

8. A method as in claim 7 wherein one of R₁ and R₂ is



wherein the alkyl group contains 1–15 carbon atoms and the other is



and R₃ is hydrogen.

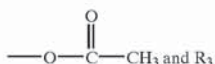
9. A method as in claim 6 wherein the leukemia is acute myelocytic leukemia.

10. A method as in claim 9 wherein in the compound of the Formula I, R₁ is

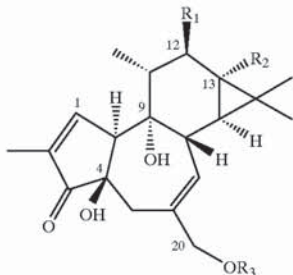


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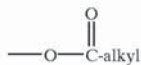
 R_2 isand R_3 is hydrogen.

11. A pharmaceutical composition suitable for parenteral administration to humans which comprises from about 0.05 mg, to about 1.5 mg, of a Compound of the Formula

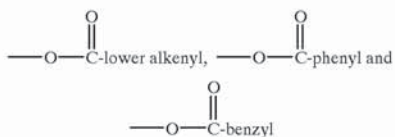


or isomers thereof

wherein R_1 and R_2 are selected from the group consisting of hydrogen



wherein the alkyl group contains 1-15 carbon atoms,



and substituted derivatives thereof, and at least one of R_1 and R_2 is other than hydrogen and R_3 is selected from the group consisting of hydrogen and

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and a pharmaceutically acceptable carrier for a Compound of the Formula I.

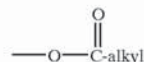
12. A composition in claim 11 wherein the carrier is an aqueous medium.

13. A composition as in claim 12 which contains from about 0.05 mg to 1.0 mg of a Compound of the Formula I.

14. A composition as in claim 12 which contains from about 0.05 mg to about 0.6 mg.

15. A composition as in claim 13 wherein one of R_1 or R_2 is

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20 and the other is



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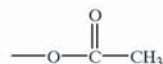
and R_3 is hydrogen.

16. A composition as in claim 14 wherein R_1 is

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 R_2 is

35



40 and R_3 is hydrogen.

17. A composition as in claim 11 wherein at least one of R_1 or R_2 is decanoate or myristate.

18. A composition as in claim 11 wherein the Compound of the Formula I is present in dosage amounts of 0.10 mg, 0.25 mg or 0.50 mg.

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19. A composition as in claim 18 wherein the dosage form for parenteral administration is an ampoule.

20. A composition as in claim 19 wherein the Compound of the Formula I is phorbol-12-myristate-13-acetate.

* * * * *

EXHIBIT D

DECLARATION OF JON BERGLIN

I, JON BERGLIN, declare as follows:

1. I am over eighteen years of age and am not a party to this action. I have personal knowledge of the facts stated below and could testify competently to them if required.

2. I am currently the Chief Executive Officer of Theragene, Inc., a Delaware corporation, dba Therinova Development ("Theragene"). Theragene began doing business as Therinova Development in approximately 2011. I have been the Chief Executive Officer of Theragene / Therinova since August 30, 2006.

3. My first contact with Ben Chang was in late July or early August 2013, when Steve Davis introduced me to Ben Chang over email.

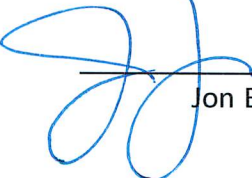
4. On or about August 21, 2013, Ben Chang provided me a variety of documents for the purpose of preparing a proposal for filing documents with the United States Food and Drug Administration ("FDA") on behalf of Rich Pharmaceuticals, Inc., including the submission of an Investigational New Drug Application as it relates to TPA and/or PD-616. Attached hereto as **Exhibit A**, Bates Nos. THER0001 to THER00081, are true and correct copies of my email correspondence, along with any files attached to those emails.

5. The bates ranges starting from THER00015 thru THER00081 in **Exhibit A** are true and correct copies of my correspondence and emails with Ben Chang and David Chou, as well as the files attached to those emails.

6. Attached hereto as **Exhibit B**, Bates Nos. THER00082 to THER0004330 are documents that I received from Ben Chang on or about August 21, 2013. These documents were delivered to me in person via flash drive by Ben Chang. The flash drive was plugged into Ben Chang's computer and the files were uploaded. I then transferred the files from the flash drive to my laptop and uploaded them to a Dropbox folder.

7. Even though I reviewed the documents attached as **Exhibit B**, Theragene never submitted any documents to the FDA on behalf of Rich Pharmaceuticals, Inc. That is because Rich Pharmaceuticals, Inc. ("Rich Pharmaceuticals") never executed the Master Services Agreement ("MSA") found at **Exhibit A**, Bates Nos. THER00019 to THER00036.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct. Executed this 21st day of February 2014, at San Diego, California.



Jon Berglin

EXHIBIT E

*Source: Rich Pharmaceuticals, Inc.
April 30, 2014 07:00*

Rich Pharmaceuticals Provides Financing Update

BEVERLY HILLS, Calif., April 30, 2014 (GLOBE NEWSWIRE) -- Rich Pharmaceuticals, Inc. (OTCQB:RCHA) ("Rich" or the "Company") is pleased to announce the completion of additional financing of approximately \$400,000 to fund the continued growth of the Company.

The proceeds from the financings will be used by the Company to commence manufacturing the drug, to engage a Contract Research Organization (CRO) to assist the Company with the preparation and filing of an IND (investigation new drug) submission to the Food and Drug Administration (FDA), and for legal, patent and administrative related expenses. The Company has raised \$310,000 in 2014 through the sale of stock and warrants to three accredited investors, and the Company has also raised \$90,500 through the issuance of convertible promissory notes.

"We continue to move forward to advance the development of our leading compound for the treatment of Acute Myelocytic Leukemia," said Ben Chang, Chief Executive Officer of the Company.

About Rich Pharmaceuticals:

Rich Pharmaceuticals, Inc. (OTCQB:RCHA) is a Biopharmaceutical Company developing a treatment for Acute Myelocytic Leukemia (AML)/white blood cell elevation and other blood related diseases. Rich Pharmaceuticals' goal is to extend refractory patients life expectancy and increase quality of life. Rich Pharmaceuticals' primary development stage product candidate which is being designed to treat blood and cancer related diseases through none evasive outpatient facilities. Find out more at www.richpharmaceuticals.com.

Notice Regarding Forward-Looking Statements:

This news release contains "forward-looking statements" as that term is defined in Section 27(a) of the Securities Act of 1933, as amended, and Section 21(e) of the Securities Exchange Act of 1934, as amended. Statements in this press release that are not purely historical are forward-looking statements and include any statements regarding beliefs, plans, expectations or intentions regarding the future. Such forward-looking statements include, among other things, references to novel technologies and methods, our business and product development plans, our financial projections or market information. Actual results could differ from those projected in any forward-looking statements due to numerous factors. Such factors include, among others, the inherent uncertainties associated with developing new products or technologies and operating as a development stage company, our ability to raise the additional funding we will need to continue to pursue our business and product development plans, our ability to develop and commercialize products based on our technology platform, competition in the industry in which we operate and market conditions. These forward-looking statements are made as of the date of this news release, and we assume no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements. Although we believe that any beliefs, plans, expectations and intentions contained in this press release are reasonable, there can be no assurance that any such beliefs, plans, expectations or intentions will prove to be accurate. Investors should

consult all of the information set forth herein and should also refer to the risk factors disclosure outlined in the reports and other documents we file with the SEC, available at www.sec.gov or under the "Investor" tab at www.richpharmaceuticals.com.

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